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PEPTIC ULCERS AND THE INTERBRAIN[1]

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THE generous founder of this lectureship, Dr. Donald Balfour, has recently reported the results of one thousand and more surgical procedures on the stomach and duodenum as conducted during the year 1930 in the famous Clinic to which he is attached. Sixty-five per cent of the operations were for acute, subacute, or chronic, gastric, duodenal, or gastrojejunal ulcers. Since it is reasonable to assume that only a small proportion of the patients with peptic ulcers of one sort or an other that sought advice during this period were operated upon,[2] these figures indicate that the condition represents one of the most common maladies of the present day.

Until roentgenology and the opaque meal came to add a measure of precision to our clinical diagnoses, many ulcers naturally enough went unrecognized during life, but it is highly unlikely that they should have been similarly overlooked by pathological anatomists by whom forty years ago duodenal ulcer, at least, was looked upon as a rare disorder. What my colleague, Dr. Christian, has recently pointed out[3]—that the incidence of many maladies, commonly seen in his wards during the past fifteen years, has remained stationary or fallen off whereas gastric and duodenal ulcer has increased four-fold—can scarcely be ascribed wholly to improved methods of diagnosis.

Since the characteristic local lesion may be the only discernible evidence of disease to be disclosed after death, it has naturally enough been ascribed to purely local causes—vascular, traumatic, bacterial, biochemical or secretory. By various ingenious experimental devices, many have succeeded in producing acute peptic ulcers or erosions in the lower animals, and under certain circumstances the mucosal defects thus produced fail to heal. But it is only in man that ulcers occur spontaneously with any considerable frequency, and it is not at all improbable that the prevalence, particularly of duodenal ulcers, has something to do with the strain and stress of modern life; for people today rarely find it possible to lead the comparatively placid existence enjoyed by their forebears.

All clinicians are familiar with the facts: (1) that "highly strung" persons are particularly susceptible to "nervous indigestion" and associated ulcer; (2) that ulcers become symptomatically quiescent or even tend to heal when patients are put mentally and physically at rest; and (3) that symptoms are prone to recur so soon as the victim of the disorder resumes his former tasks and responsibilities. Though this emotional or psychic aspect of

[2] In a later issue of the weekly *Proceedings of the Mayo Clinic*, for October 7, 1931, Dr. H. R. Hartman states that in 1928 the diagnosis of gastric or duodenal ulcer was made in 2,499 patients. In 2,015 instances (90 per cent), the lesion was duodenal, in 224 instances (10 per cent) gastric, and in 27 cases (1 per cent) both gastric and duodenal ulcers were present. Of the duodenal ulcers, 797 (or 39 per cent), and of the gastric ulcers 155 (69 per cent), were operated upon.

[3] Sixteenth Annual Report of the Peter Bent Brigham Hospital for the year 1929, p 139.

[1] Being the basis of the fourth Balfour Lecture, given a year ago at the University of Toronto, April 8, 1931.

the ulcer problem has been frequently emphasized in the past, the locus of the primitive emotions and their relation to parasympathetic discharges and vagotonia has only come to be partly understood in recent years. It is proper, therefore, at the outset to disclaim any pretense toward a novel explanation of the pathogenesis of ulcer. At the same time, the hope is expressed that what will be forthcoming may serve in a measure to reconcile the several conflicting hypotheses, many if not all of which doubtless contain certain elements of truth.

What has incited my interest in the subject has been the disturbing experience of having lost three patients from acute perforations of the upper alimentary canal soon after what appeared to be successful operations for the removal of intracranial tumors; and that each of these tumors happened to be situated in the cerebellum could not, it seemed to me, be other than of some significance. How to explain these occurrences was the difficult problem and in the attempt herein to do so, I may best proceed by first giving an account of the three distressing episodes.

I. CASE REPORTS

a. Acute Postoperative Perforations

These, as stated, in all three instances followed suboccipital operations for cerebellar tumors.

CASE 1. (P. B. B. H. Surgical No. 3055.[1]) *Cerebellar symptoms of six months' duration. Suboccipital exploration under ether anæsthesia. Enucleation of subcortical angioblastoma from right cerebellar hemisphere. Acute abdominal symptoms. Death in 24 hours from general peritonitis due to multiple perforations of the stomach.*

June 11, 1915. On the advice of Dr. C. C. Burpee, of Malden, Massachusetts, the patient, Alvar C., aged 34 years, a bank clerk, was admitted to the Brigham Hospital because of a choked disc and other evidences of brain tumor.

Past history. He had had scarlet fever as a child complicated by an otitis media; also an attack of typhoid when aged 20 years, but otherwise had always enjoyed good health until the onset of his present symptoms. He had been married nine years, had raised a family and was a man of exemplary habits.

[1]This case has been briefly reported in another connection: Cushing and Bailey, "Blood-Vessel Tumors of the Brain," C. C. Thomas, 1928, Case XVII, page 124.

Anamnesis. In *December, 1914*, six months before admission, he began having suboccipital headaches followed ere long by failing vision. In *March, 1915*, his gait became unsteady and a month later he began to have attacks of morning vomiting accompanied by nausea. Diplopia, dizziness, and tremor of the hands had also been recently observed.

Physical examination. Apart from the neurological signs, which were unequivocally those of a right cerebellar tumor with secondary hydrocephalus and choked disc, the examination was wholly negative. Regarding the abdomen, the record states that "no masses were seen or felt; no tenderness, muscle spasm or rigidity. Spleen and kidneys not palpable. Liver dullness extends to costal margin in midclavicular line. Percussion note everywhere tympanitic."

Operation. June 17, 1915. 10 a.m. The patient was placed face-down in a comfortable position on the cerebellar table and anæsthetized by warm ether vapor, the Connell apparatus being used for its delivery through a nasal tube. The usual bilateral suboccipital exploration was made with exposure of both cerebellar hemispheres and removal of the bone comprising the posterior half of the foramen magnum. To lower tension the left lateral ventricle was punctured before opening the somewhat tense dura. On reflecting the membrane a superficially placed, evidently benign tumor was disclosed in the center of the right cerebellar field. The tumor, about the size of a golf ball, was readily enucleated intact owing to its smooth surface and definite capsule. The bleeding was trifling and easily controlled by a few clips. The wound was closed carefully in layers in the usual detail.

The anæsthetic had been given by Dr. W. M. Boothby with the Connell apparatus and was smoothly taken. The operation lasted just short of three hours and at its conclusion the patient was in good condition and there seemed to be no reason to expect anything other than an uneventful recovery.

Subsequent notes. On first regaining consciousness (1.30 p.m.), while still in position on the operating table, the patient complained of feeling chilly and of abdominal discomfort. He vomited more than usual (a bile-stained fluid) and his bowels moved freely, the stool containing mucus streaked faintly with blood. After he was removed from the table at 3.30 p.m., he complained of increasing abdominal pain; the belly seemed somewhat stiff and tender to palpation but no especial significance was attached to the fact. During the rest of the afternoon, he continued occasionally to retch, vomit, belch, and pass gas per rectum. He had also a peculiar grunting expiration which, however, was regular and without Cheyne-Stokes' rhythm.

He was finally taken to the ward at 6 p.m. His rectal temperature was then 102.4 degrees. Owing to restlessness and further complaints of abdominal pain, he was given at 8.30 p.m. a sixth of a grain of morphia subcutaneously. Not long after this his pulse and respiration began to quicken and at 10.30

p.m. to quiet him he was given another one-sixth of morphia. From this time onward he became progressively worse; at 1.00 a.m. his rectal temperature was 104 degrees. His appearance an hour later, when I was called to see him by my then assistant, Dr. E. B. Towne, reminded me of a state of "hyperthermic shock," whatever was meant by that.

My personal notes state: "2 a.m. He is conscious, alert and subjectively comfortable but breathing rapidly with an expiratory grunt; no rhythmicity about respiratory act; pulse very irregular, often barely perceptible and uncountable at the wrist. Extremities cold and clammy though he says they feel hot."

And again at: "5 a.m. Has slept off and on the past three hours on his morphia. No change in general condition. Has voided. Difficult to tell what is wrong. He is mentally clear and cheerful. The abdomen is slightly distended and so sensitive it cannot be touched without making him wince. This superficial tenderness suggests some spinal cord (referred pain) complication. To exclude the possibility of a postoperative clot a lumbar puncture has been made. Fluid found clear and not under tension."

"6.30 a.m. Definitely failing though remains conscious and clear. Pulse barely perceptible. The condition now looks more like a *general peritonitis* as from a perforative ulcer, a mesenteric thrombosis, or acute obstruction (though no vomiting since morphia) than any intracranial condition with which I am familiar."

He grew increasingly worse, became cyanotic and nearly pulseless and the end came at 10.15 a.m., just twenty-four hours after the start of the operation.

[It was subsequently learned from the patient's wife that on the day before his operation he had eaten some cake, brought to him by a visitor, and this had disagreed with him. Indeed, so long as she had known him, he had always had a poor digestion and would frequently regurgitate food "like a baby with an overfilled stomach." In 1903, he had had an attack supposed to be appendicitis with "stoppage" from which he had recovered without operation after discharging some dark material by the bowel.]

Postmortem examination (Dr. J. L. Stoddard). The unrestricted autopsy was held at 1.15 p.m., three hours after death. Apart from the recent operative wound the intracranial conditions were normal. There was no evidence of clot or postoperative œdema.

The peritoneal cavity contained a large amount of turbid fluid with a generalized acute fibrinous peritonitis particularly marked in the upper abdomen. The stomach showed three circular perforations half way between the cardia and pylorus on the lesser curvature (Fig. 1, frontispiece). About these perforations there were no indurations or indications of inflammatory reaction. On opening the stomach an acute process was disclosed resembling the acute gastritis of a corrosive poisoning. There were widespread submucosal hæmorrhages and the mucous membrane in many places was so damaged the organ could readily have been torn by the fingers. The process was more marked in the cardiac half of the stomach and the lower portion of the œsophagus was likewise involved with longitudinal slits in the mucous membrane and submucosal hæmorrhages. In certain areas, as at the site of the three perforations, the wall was actually necrotic throughout.

Microscopical examination (Prof. W. T. Councilman): *Stomach.* Sections from the involved areas showed a normal mucosa with no degeneration of the glands though in places there was a slight infiltration with polynuclear cells. Sections from the margins of the mucosal rents showed evidence of hæmorrhage into the coats as though torn by mechanical violence. The punctate areas in the fundus proved to be shallow, hæmorrhagic erosions (Fig. 2) with marked œdema of the submucosa and a heavy infiltration of polymorphonuclear leucocytes involving all coats, even to the serosa, unmistakably an antemortem process.

In his further discussion of the case, Dr. Councilman expressed the belief that inflation of the stomach by ether vapor had produced the rents in the mucosa. This view was regarded, however, as highly improbable for the Connell apparatus, which gives a measured percentage in tension of warmed ether vapor, had been utilized without accident of the sort in thousands of cases, many of them patients with cerebellar tumors. Several other possible explanations were considered: (1) for an acute corrosive poisoning there was no apparent source; (2) an agonal digestion of the stomach wall did not accord with the clinical evidences of peritonitis long before death; (3) the patient's face-down position for many hours on the operating table was considered as a possible cause only to be discarded.

At about this time, G. M. Smith [1] had shown that hæmorrhagic ulcerations or erosions with necrosis could be easily produced when a combination of bile and 5 per cent hydrochloric acid were experimentally injected into the fasting stomach of animals. There had been no occasion to make a gastric analysis of the patient before the operation, but the history subsequently elicited suggesting

that he had suffered from hyperacidity coupled with the fact that on recovery from the anæsthetic he had vomited an abundance of bile-stained fluid seemed therefore to offer the most plausible explanation of the lesions.

This harrowing experience, unsatisfactorily accounted for, was wellnigh forgotten when twelve years later it was vividly recalled by the series of events in the following case:

CASE 2. (Surgical No. 30113.) *Cerebellar-tumor symptoms of five years' duration. Suboccipital exploration under local anæsthesia temporarily supplemented by ether. Incomplete electrosurgical extirpation of huge astrocytoma. Prolonged operation. Acute abdominal symptoms three days later with death on fourth postoperative day. Autopsy: multiple acute perforations of duodenum.*[1]

George M., an engineer, 34 years of age, was admitted *November 16, 1927*, with the full blown picture of a cerebellar tumor. Symptoms had occurred with the following chronology: For five years, dizziness on stooping with subsequent blurring of sight, also suboccipital stiffness and tenderness; for three years, occasional attacks of vomiting without nausea; for two years, increasing dysarthria and dysphagia, ascribed to the extraction of teeth; for eighteen months, loss of visual acuity; for ten months, staggering gait; for six months, increasing weakness of the right side; for three months, occasional "cerebellar fits" with retraction of neck, sweating, dizziness, and temporary unconsciousness; for two months, periodic diplopia.

Examination. This showed: a bilateral choked disc of 5 diopters; marked ataxia and slight hypæsthesia of all extremities; sustained nystagmus to either side; left abducens palsy; marked static instability with tendency to deviate to the right; suboccipital tenderness; right astereognosis; dysphagia and dysarthria.

Operation. November 29, 1927. The cerebellum was exposed by the usual bilateral crossbow incision with puncture of the dilated lateral ventricles. A median tumor was disclosed which grossly resembled an ependymoma but which proved to be a fibrillary astrocytoma. It had a long tongue projecting so far into the spinal canal that a laminectomy of the axis as well as of the atlas was necessary in order to expose its lower pole (Fig. 3). This forbidding growth was radically attacked but its extirpation was finally abandoned short of completion owing to respiratory difficulties set up by manipulations of the residual fragment which overlay the posterior floor of the ventricle.

The operation was started at 10.30 a.m. under novocain anæsthesia; at 12.50 p.m., because the handling of the tumor was causing the patient distress, inhalation narcosis was substituted. Owing to the tough, rubbery character of the growth it was removed piece-meal by electrosurgical methods, and the current was frequently in use during the three hours from 12.50 to 3.50 p.m. while the patient was under ether. The wound closure was not completed till 5.30 p.m. by which time consciousness had been wholly regained.

Postoperative course. The patient was kept on the cerebellar table during the next several hours, for though his general condition was satisfactory, this position enabled the mucus and saliva, which he had difficulty in swallowing, to drain from his mouth. In two hours the rectal temperature had risen to 104.8 degrees. He was sponged and the temperature fell. At 11 p.m., he was removed from the table to bed. By 7.30 a.m., the next morning, he was thought to be out of danger and was returned to the ward: pulse 110, respirations 12, rectal temperature 101 degrees. He took liquid nourishment well though the pre-operative difficulty in deglutition was evidently increased. A lumbar puncture was performed, 35 cubic centimeters of blood tinged fluid not under tension being removed.

His condition appeared in every way to be satisfactory during the next two days until 4.15 p.m., *December 2*, when he had a sudden violent epigastric pain which spread over the abdomen and into the shoulders. This was ascribed to a probable pleuritis and an attendant thought he heard a friction rub in the right anterior axillary line. Rectal temperature was 102.4 degrees. He soon became exceedingly restless and was given 10 milligrams morphia, which quieted him. The temperature continued to rise during the night and at 5.30 a.m., *December 3*, had reached 106.2 degrees. There had been no vomiting and no suspicion of an acute abdominal complication was at any time aroused. The radial pulse became imperceptible and he died at 8.15 a.m. on this, the fourth postoperative day.

Postmortem examination 4 hours after death (Dr. G. A. Bennett). The brain showed a residual mass of non-adherent tumor deeply indenting and flattening the medulla (Fig. 4). The lungs apart from slight hypostatic congestion were normal in appearance.

The *peritoneal cavity* was found to contain 1100 cubic centimeters of a dark reddish-brown fluid. When this was removed a generalized diffuse fibrinoplastic peritonitis was disclosed. On separating the intestines which were held together by the sticky fibrinous exudate two perforations of irregular shape, through which the contents of the bowel were easily expressed, were found in the wall of the duodenum about 3 centimeters distal to the pylorus (Fig. 5). The larger opening measured roughly 12 by 14 millimeters, the smaller 9 by 8 millimeters. Neither of them was indurated or showed evidence of a chronic inflammatory process. About 5 centimeters farther down the duodenum were two shallow ulcerations or erosions in the mucous membrane, the larger of them measuring 8 by 4 millimeters in diameter. The

[1] In a report on the cerebellar astrocytomas (Surg., Gynec. & Obst., 1931, lii, 129-204), this is Case 53.

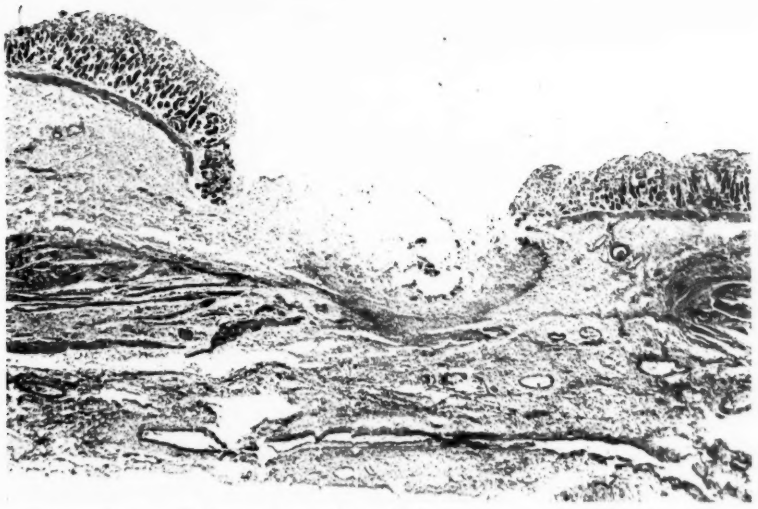

Fig. 2. Case 1. Typical punctate hæmorrhagic erosion extending through submucosa (mag. × 15).

gastric mucosa, the ampulla of Vater, the pancreas, and its ducts were all of normal appearance.

Microscopical examination. Sections at the margins of the perforated areas showed merely a loss of structure with marked œdema and fibrin deposition. Those taken through the erosions showed a completely destroyed mucosa which was replaced by an exudate of fibrin, inflammatory cells, and blood; the submucosa and to some extent the muscularis were œdematous and heavily infiltrated with polymorphonuclear leucocytes, lymphocytes, and fibroblasts. Homogeneous blue-staining thrombi, in which polymorphonuclear leucocytes were incorporated, were present in the capillaries, small arteries, and veins, both of muscularis and submucosa. Occasional arteries of considerable size were surrounded by coarse meshed fibrin. These features, in the opinion of the pathologists, were those constantly seen in duodenal ulcer and indicated that vascular thrombosis was the local cause of the lesions which were unmistakably antemortem in origin.

The operation in this case, as events proved, was ill judged, for the patient might have recovered had the tumor been left alone and the chance taken of providing symptomatic relief by decompressive measures. But this source of regret lies apart from the present discussion. What concerns us is the fact that here again was a fatality from a perforative peritonitis, wholly unsuspected during life. The attack of acute abdominal pain, which doubtless ushered in the process, was wrongly ascribed to a probable pulmonary complication brought about by the patient's deglutitory difficulties.

As in the first case, in an effort to explain the multiple perforations which here, to be sure, were duodenal rather than gastric, it was necessary again to consider: (1) the man's face-down position on the table; (2) the prolonged operative procedure; (3) the three-hour period of ether anæsthesia with the Connell apparatus; and (4) the possibility of trauma in lifting the patient from the table. There, moreover, was the additional element of the powerful electrosurgical current that had been used with the negative electrode against the abdomen, the possible complications from which, in 1927, were unknown to us. Time, however, has shown from a multitude of other experiences that diathermy does not damage the nervous tissues, and though we have once seen a superficial burn due to imperfect contact of the large negative electrode against the skin, no other ill effects have ever been observed.

Here, then, was another distressing experience following a cerebellar operation with an early postoperative fatality due to multiple duodenal perforations for which there was no ready explanation. The account of a third episode of similar kind follows.

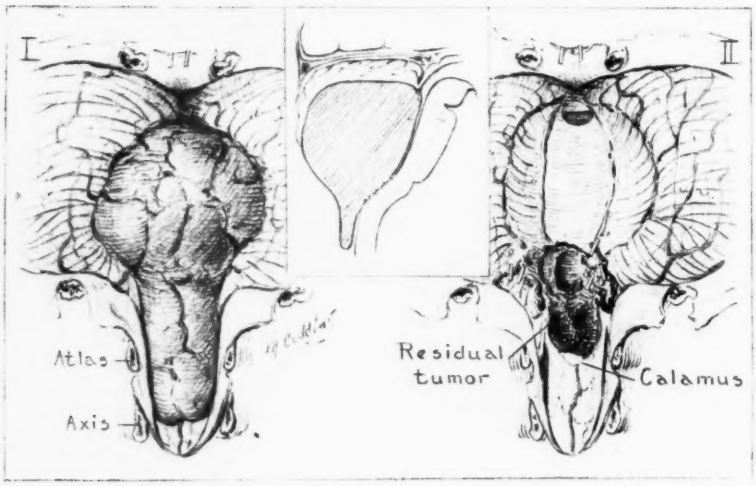

Fig. 3. Case 2. Showing: *I*, Median astrocytoma with spinal tongue necessitating laminectomy of both atlas and axis for its exposure; *II*, the resicual part of the tumor.

wound. The child's radial blood pressure during the last hour was too low to be registered but a transfusion of blood was given with prompt improvement. The extirpation was necessarily left incomplete but it was hoped that enough of the growth had been removed temporarily to relieve pressure symptoms while radiotherapeusis could be employed.

On the following day, *January 27*, fearing from the child's symptoms that a clot might have formed, at 11 a.m. the entire wound was reopened under local anæsthesia. At this session great masses of highly infiltrated tumor which were extruding from the cavity were removed with further loss of blood necessitating a second transfusion which promptly restored the fallen pressures.

During the remainder of this second day and night, the child seemed much improved and there was hope of recovery. Apart from the occasional vomiting of brownish "coffee ground" fluid, which caused us to apprehend a possible erosion of the gastric mucosa, conditions seemed favorable until 6 a.m. on *January 28* when there was a sudden rise of temperature to 104.4 degrees. This was associated with labored respiration, bronchial râles and considerable cyanosis. Two hours later the temperature had risen to 106 degrees. There was copious vomiting of brownish black fluid.

On the remote chance that the unfavorable turn was due to a clot or to a further dislodgment of infiltrated tumor, the wound at 9.15 a.m. was again quickly opened and closed without anything being found to account for the symptoms. A third transfusion was given with imagined improvement but this was temporary and the child died at 1.40 p.m., with a temperature of 106 degrees, some 50 hours after the first operation.

Autopsy one hour after death; unrestricted (Dr. R. Z. Schulz). The brain showed a large residual mass of the tumor which extended up into the lateral recess alongside the brain stem and projected through the incisura tentorii flattening the side of the pons (Figs. 6 and 7). There was a secondary hydrocephalus of high degree. The tumor proved to be a medulloblastoma.

In the further progress of the examination, the peritoneal cavity and the subdiaphragmatic organs

Case 3. (Surgical No. 30532.) *Highly advanced cerebellar syndrome in a child. Suboccipital operation under ether with incomplete removal of large vascular medulloblastoma. Transfusion. Postoperative dysphagia with vomiting of brown fluid. Wound reopened with second transfusion. Autopsy: Perforation of œsophagus with digestion of mediastinal tissues.*

January 23, 1928. On the recommendation of Dr. John L. Eckel of Buffalo, Joseph C., 10 years of age, was admitted as an emergency with the unmistakable signs of a cerebellar tumor. The symptoms in their order of onset were as follows: For two or three years clumsiness, instability and ataxia; for six months, increasing dysarthria; for three months, suboccipital headaches and vomiting; for one month, tinnitus and internal squint.

Examination showed a bedridden child with an enlarged head, a secondary optic atrophy with near blindness; a persistent wandering nystagmus; a left abducens palsy; paresis of left facial nerve; slurring of speech; marked ataxia, hypotonicity and hypermetria of all extremities with absent deep reflexes.

Operation. January 26th. 10.40 a.m. As the child was too ill and unco-operative for local anæsthesia, gas-ether was employed. The suboccipital approach was exceedingly difficult and bloody. In spite of a preliminary ventricular puncture, so soon as the left cerebellar hemisphere was exposed a huge median tumor began to extrude through the thin overlying cortex. The growth was so vascular, it was mistaken for an angioma cavernosum. It was impossible to do more than to scoop and suck out what appeared to be the chief mass of the growth and to control bleeding by electrosurgical methods and temporary packing. It was a desperate procedure and not until four hours had elapsed was it thought safe to close the

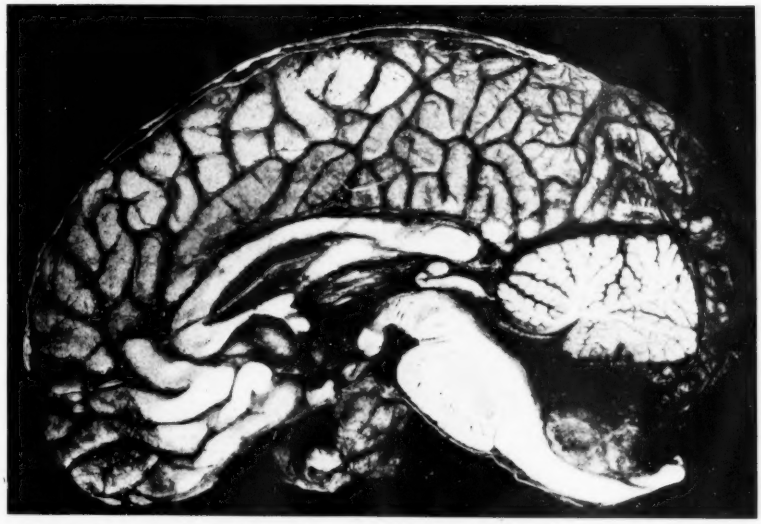

Fig. 4. Case 2. Showing flattening and indentation of the medulla by residual fragment of the non-adherent tumor.

were found to be normal in all respects; this was true also of the right chest. The left pleural cavity, however, was largely filled by dark brownish fluid of precisely the same type that the patient had occasionally vomited; floating on its surface was a considerable amount of free fatty material and whitish débris. When, after removal of the fluid, the normal-appearing and crepitant lung was tilted forward, it could be seen that the pleura, over a large area including the side of the pericardium, the dome of the diaphragm, the bodies of the vertebræ and posterior thoracic wall, had been digested away together with the fat and areolar tissue of the mediastinal space. This left the aorta and its branches, the mediastinal nerves, the vertebræ, and the œsophagus cleanly exposed as in a dissection (Fig. 8). In the side of the œsophagus was a ragged hole about 3 centimeters in length from which, on compressing the stomach, the same brownish material found in the chest could be expelled.

Specimens of the free fluid after filtration showed a total acidity percentage of 52, which is about the upper limit of normal for free and combined acids in gastric contents. A piece of omental fat *circa* 5 centimeters in diameter was incubated in 40 cubic centimeters of the fluid and in 48 hours had disappeared, many fat globules remaining on the surface. A piece of muscle similarly treated was reduced to about a fifth of its original size in 72 hours.

Microscopical examination of the lower œsophageal wall showed a highly œdematous and partly autolyzed tissue containing occasional erythrocytes and an abundance of polymorphonuclear leucocytes.

Here, as in the two preceding cases, there were definite antemortem evidences of the lesion. The dark colored vomitus suggested an erosion somewhere in the upper alimentary canal, but the absence of all abdominal signs threw us wholly off the track, an œsophageal perforation being unsuspected.

This startling experience was reminiscent of that in the two foregoing cases only for the reason that the antecedent operations had also been for a cerebellar tumor. Otherwise, there might have been no inclination to seek a common explanation for the three episodes, particularly since the perforative lesion occurred in a different situation in each instance. This child at the time of operation was in a seriously enfeebled condition and in view of the subsequent hyperthermia might well enough have had an agonal digestion of the œsophagus; and this was the contemporary belief expressed by the pathologists. Œsophageal perforations of like kind I recall having occasionally seen years ago at autopsies on typhoid-fever victims, it having been assumed that the perforation was due to regurgitation of gastric contents into the œsophagus; and to non-perforative ulcers of this same origin the once not uncommon post-typhoidal strictures of the œsophagus were formerly ascribed. It is, of course, known that true peptic ulcers may occur in aberrant islands of gastric mucosa [2] in the lower œsophagus just as they may occur in the patches of gastric mucosa in the presence of Meckel's diverticula [3 ; but these anomalously situated lesions, though they may have some bearing on the subject, lie apart from the present discussion.

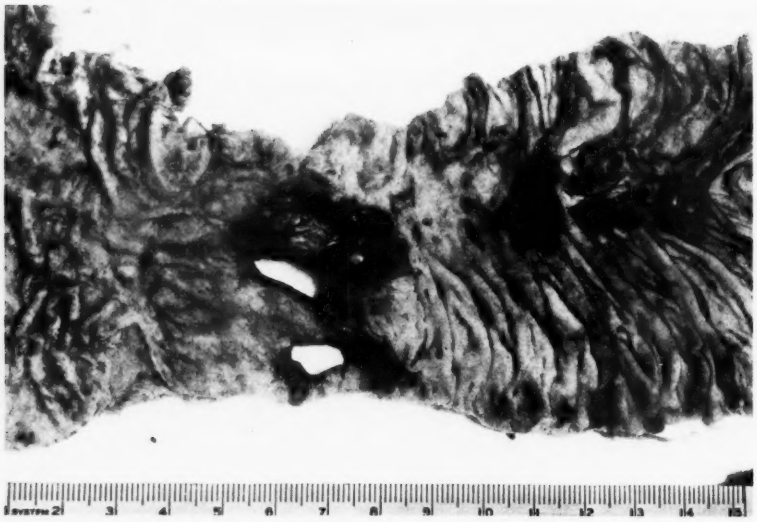

Fig. 5. Case 2. Showing (slightly reduced) the perforations and erosions of the duodenum.

In each of these three cases, furthermore, there were antemortem symptoms: shown in Case 1 by acute abdominal pain, tenderness, and distention which preceded death by twenty hours; in Case 2 by sudden acute upper abdominal pain sixteen hours antecedent to death; and in Case 3 by the vomiting of fluid discolored by changed blood and by respiratory disturbances for some twelve to fourteen hours before death. The operations in Cases 2 and 3 were highly critical procedures that must seriously have drawn upon the patient's resistance, but this was not true of the operation in Case 1. From these three observations, it is altogether natural to assume that erosions, which may not go on to actual perforation, are possibly of more frequent occurrence after operations for brain tumor than is commonly supposed. To this question we may now turn.

b. Antemortem Mucosal Erosions

Mucosal erosions whether they happen to be hæmorrhagic in type or conform to the so-called stigmata of Beneke [4] are well known to pathologists. They were fully described by Carl Rokitansky, and Samuel Wilks in his celebrated "Lectures on Pathological Anatomy" stated [5]:

> "We occasionally meet with small gastric ulcers, perhaps entirely unsuspected in the fatal illness, the symptoms having been overwhelmed by those of the main disease. These we have seen as single, reniform, or circular erosions, generally near the pylorus; sometimes they are quite shallow, and a little blood extravasated in the mucous membrane around would give rise to the suspicion that hæmorrhage into the tissue, weakening it and leading to its solution, may be a cause of such ulcers."

The circumstances that permit one to demonstrate mucosal erosions after an intracranial operation are not often combined: namely, (1) an operation of the sort to produce them; (2) a postoperative fatality at the proper time to find them, for the multiple small erosions such as may be produced by a great variety of experimental methods are known to heal over quickly; (3) permission, after a fatal operation on the brain, for an unrestricted autopsy; and (4) a more careful scrutiny of the gastroduodenal mucosa than is customary, particularly when the obvious cause of death lies elsewhere.

The absence of one or another of the four necessary factors mentioned may in part explain how it is that only two examples are here recorded. One of them happened to be come upon while making a statistical study of the cerebellar astrocytomas a few years ago.

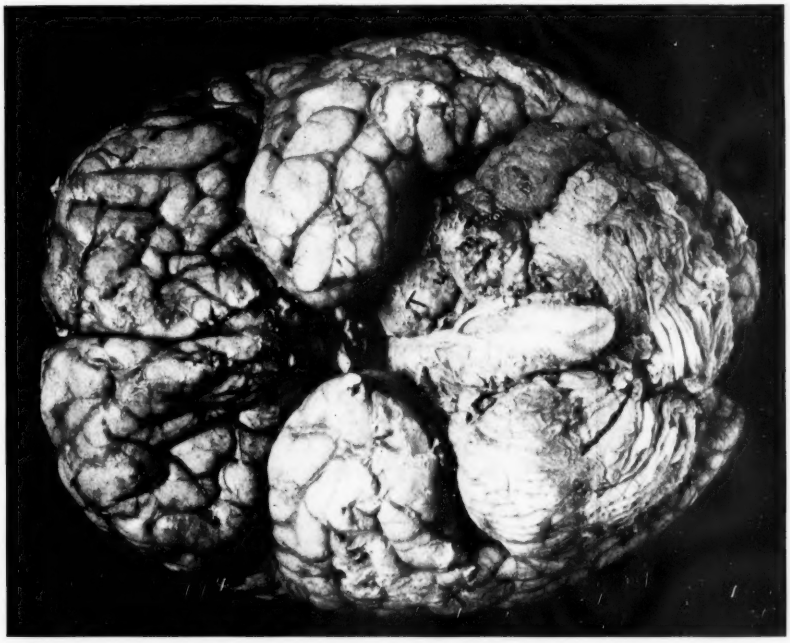

Fig. 6. Case 3. Showing residual tumor mass (medulloblastoma) extending into left lateral recess.

CASE 4. (Surgical No. 664.) *Recurrent cerebellar astrocytoma. Death after third operation due to streptococcal meningitis. Hæmorrhagic erosions of stomach noted at autopsy.*

A child, six years of age, with an advanced cerebellar syndrome and blindness first came under observation at the Johns Hopkins Hospital; and on *May 24, 1910*, a large cerebellar cyst was opened and drained with freedom of symptoms for a year. On *August 3, 1911*, a large, recurrent, cystic tumor was partially removed by the late Dr. E. H. Nichols of Boston, again with a good temporary recovery. On *December 8, 1913*, she was admitted to the Brigham Hospital for recurrence of symptoms, among which occipital headaches, projectile vomiting, and constipation were prominent. At a third operation, a solid tumor mass was removed, the child dying six days later from a streptococcal meningitis with a temperature of 107 degrees.

The protocol of the autopsy, held 3½ hours after death, states that: "Near the cardia along the greater curvature are found several areas where the mucous membrane is lacking, the largest measuring 3 millimeters in diameter. The bases of these ulcers (*sic*) are reddened as is also the fundus of the stomach."

No sections were cut and the lesions were simply recorded by painstaking observers as incidental findings.

How often similar small erosions of the gastric mucosa may occur after cranial operations is wholly conjectural, but their presence would explain why the vomitus not infrequently contains traces of blood which ordinarily is supposed to have been swallowed. The following is a recent example of erosions found at autopsy after a fatal operation for a lesion in the subfrontal rather than the cerebellar region.

CASE 5. (Surgical No. 37259.) *Extirpation of large olfactory groove meningioma. Injury to anterior cerebral arteries and fatality after 48 hours. Hæmorrhagic erosions of stomach found post mortem.*

A 53 year old mill worker entered the hospital *September 11, 1930*, on the recommendation of Dr. I. A. Farrell of Pawtucket, Rhode Island. For six months he had been working under a strain and his family learned accidentally that he had been vomiting every morning while at work and that he had shown some emotional instability. He was supposed to have a nervous breakdown. Three months later he began to have impairment of sight in the right eye with increasing weakness in the left side of the body.

Examination. This revealed an apathetic, hemiparetic man with impaired memory and some disorientation. There was an apparent left homonymous

Fig. 7. Case 3. To show (nat. size) involvement of brain stem by residual tumor.

hemianopsia to rough tests, a low grade of choked disc and loss of sense of smell in the right nostril. A diagnosis was made of a right frontal tumor, possibly an olfactory groove meningioma; this diagnosis was supported by ventriculography.

Operation. On *September 23*, under novocain anæsthesia, a large right frontal boneflap was turned down disclosing a tense dura. After reflecting this membrane and uncapping the right frontal lobe, a typical nodular meningioma of considerable size (132 grams) was disclosed. The temptation to enucleate this tumor intact rather than by preliminary excavation and piece-meal removal was not resisted. At the final moment of dislodging the solid growth (Fig. 9) from its bed, there was a sudden profuse hæmorrhage. Both anterior cerebral arteries firmly embedded in the tumor had been torn off. They were fortunately caught up in the sucker and occluded by clips before there was a serious loss of blood.

Following this operative accident the patient, as was anticipated, had a bilateral spastic paralysis of both lower extremities associated with spontaneous clonic movements. He exhibited the usual clutching and grasping reflexes in the right hand which alone retained spontaneous movements.

On the following day when the wound was dressed some slightly blood tinged cerebrospinal fluid was removed from under the flap. Because he was taking nourishment poorly a nasal tube was introduced which withdrew about 50 cubic centimeters of coffee-ground material in which erythrocytes were demonstrable by microscopical examination. On the second day his temperature suddenly rose to 107 degrees and he died in hyperthermia 48 hours after the conclusion of the operation. Shortly before his exitus he vomited a large amount of bloody fluid.

Autopsy. Permission was given for an unrestricted and immediate examination which was made twenty minutes after death (Dr. R. Z. Schulz). It was found that the tumor had been cleanly removed except for a small fragment incorporated with the stump of the right internal carotid artery. A clip had been placed apparently on the middle cerebral artery on the right side, probably also on the anterior cerebral on the left, though this could not be precisely determined.

On opening the stomach numerous flecks of coffee-ground material suggesting changed blood were found, also spots of recent hæmorrhage with small clots attached to the surface of the mucosa which was studded with numerous small punctate ulcerations varying from 1 to 3 millimeters in diameter. When looked at through a magnifying glass (Fig. 10), they proved to have slightly irregular margins. The erosions were very superficial and were found scattered everywhere, both in fundic and pyloric regions, with no site of predilection. The mucous membrane of the œsophagus and small intestine was normal in appearance.

Microscopical examination. Sections of the stomach showed numerous small mucosal hæmorrhages, some with overlying erosions and some with the mucosal surface still intact (Fig. 11). They were looked upon as essentially recent antemortem capillary hæmorrhages. The red blood cells were well preserved and there was neither deposition nor phagocytosis of blood pigment. There was no evidence of arterial or capillary disease or any noteworthy constriction or thrombosis of the vessels. Nowhere were hæmorrhages observed in the submucosa, the architecture of which was normal in all respects.

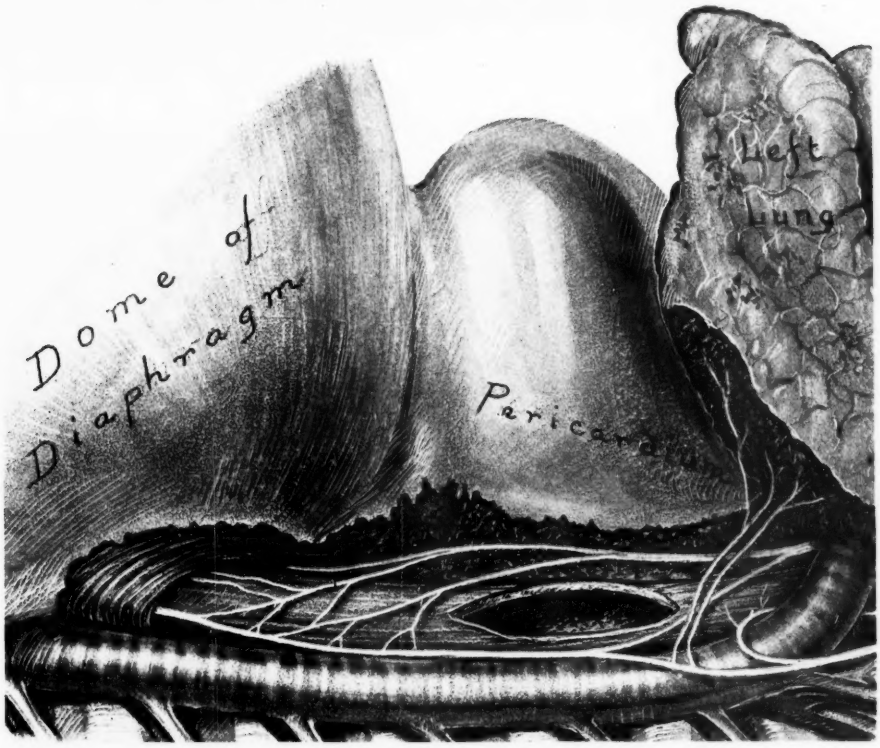

Fig. 8. Case 3. Showing position of œsophageal perforation and upper visceral margin of mediastinal digestion leaving nerves and vessels wholly naked.

Had we not been on the alert by this time (1930) for mucosal erosions after fatal operations for brain tumor wherever situated, it is safe to say that the minute lesions described might easily have escaped notice or have been regarded as of no significance. Their histological appearance coupled with the finding of demonstrable blood in the gastric contents twenty-four hours before death clearly indicates their antemortem character. Attention may be called to the fact that an olfactory groove tumor of the type described underlies the frontal lobe, and its posterior projection, overriding the optic chiasm, necessarily deforms the third ventricle. There consequently is always a risk of injuring important structures in the final dislodgment of the posterior fragments of such a growth even when it is removed piece-meal; and either from trauma or because of the vascular accident described in the operative note, the operation in this case was equivalent to a decortication of the frontal lobes. While the relation to the subject in hand of this particular fronto-diencephalic region will be fully considered later on, it may suffice at the moment to point out that the seat of the operative manipulations was far removed from that associated with the perforative lesions and erosions mentioned in the four preceding case reports.

c. Gastric Erosions and Perforation Accompanying Malignant Hypertension

Lesions similar to those already described occur in patients with intracranial conditions other than actual tumor. Two recent examples of malignant hypertension associated with choked disc may be briefly cited in

Fig. 9. Case 5. Lateral view of the olfactory groove tumor (nat. size) showing below the nodule that projected into the pituitary fossa between the anterior legs of the chiasm; also a branch of the torn anterior cerebral artery with clip.

illustration. In one of them the erosion led rapidly to perforation resembling the conical "punched ulcer" which in my student days was associated in the mind of the profession with some constitutional predisposition, more particularly with that once common disorder, chlorosis.

CASE 6. (Medical No. 37972.) *Malignant hypertension with choked discs. Moderate arteriosclerosis with cardiac hypertrophy. Hydrothorax. Death with hyperthermia. Autopsy: multiple recent gastric ulcers.*

On *November 14, 1930*, a poorly nourished, high-strung divorcée 32 years of age, supporting herself and her children as a bookkeeper, entered the hospital with a history of five months of headache, dyspnœa, palpitation, insomnia, nycturia, and indigestion, with occasional attacks of nausea and vomiting. Examination showed an enlarged heart, moderate arteriosclerosis, choked discs, a blood pressure of 270/150, and slight traces of albumin in the urine.

She developed hydrothorax, which was relieved by punctures, and in course of the next six weeks went gradually down hill in spite of all efforts to alleviate her condition. On *January 7*, she became unconscious, developed fever, remained in coma for 24 hours and after a series of convulsive seizures died at 11 a.m. on *January 8*, with a terminal temperature of 104 degrees.

Autopsy: 2½ hours after death (Dr. Hertig). The examination revealed chronic myocarditis, mild vascular nephritis, moderate general arteriosclerosis, bilateral hydrothorax, and multiple recent gastric ulcers. The gastric mucosa was found to be intensely injected and to contain numerous, small stellate-shaped recent ulcerations, more marked on the lesser curvature, to many of which fairly recent blood clots were adherent. The mucosa of the duodenum was injected but without ulcerations. The gastro-intestinal tract elsewhere presented nothing of note.

Microscopical sections of the stomach showed, in addition to the recent acute erosions, a generalized congestion with thickening of the arterioles of the mucosa (Fig. 12). The base of the ulcerative defects contained a slight amount of necrotic débris, a few polymorphonuclear leucocytes, the surrounding struma being infiltrated by leucocytes, plasma cells, and lymphocytes. The mucosa was greatly congested and many small, tightly contracted and thrombosed arteries were present both in mucosa and submucosa (Fig. 13). The larger vessels showed practically no intimal change.

In the following case—an example of the same clinical disorder—there had been an antemortem perforation of the stomach into the lesser peritoneal cavity.

CASE 7. (Surgical No. 35716.) *Malignant hypertension with choked discs. Moderate arteriosclerosis with cardiac hypertrophy. Hæmatemesis. Perforation of gastric ulcer. Operation. Death after five days. Delayed autopsy. Autodigestion of stomach.*

On *January 29, 1930*, Seth W., a somewhat obese man, aged 44 years, was transferred from the Deaconess Hospital as a brain-tumor suspect because of headaches and failing vision associated with vascular hypertension of a year's duration. He was not a "nervous" person and had never been troubled by gastric symptoms of any kind.

Examination. This disclosed choked discs of six diopters with secondary atrophy and visual acuity reduced to 20/200. The blood pressure was 210/145

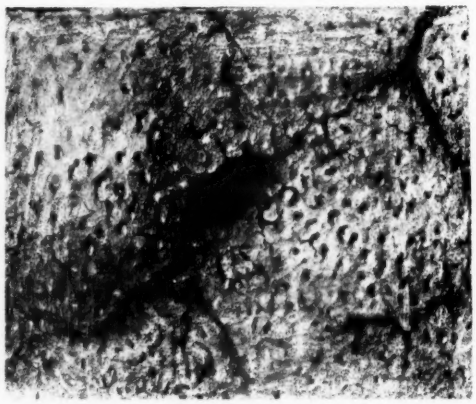

Fig. 10. Case 5. Showing (mag. × 20) the appearance of one of the punctate hæmorrhagic erosions.

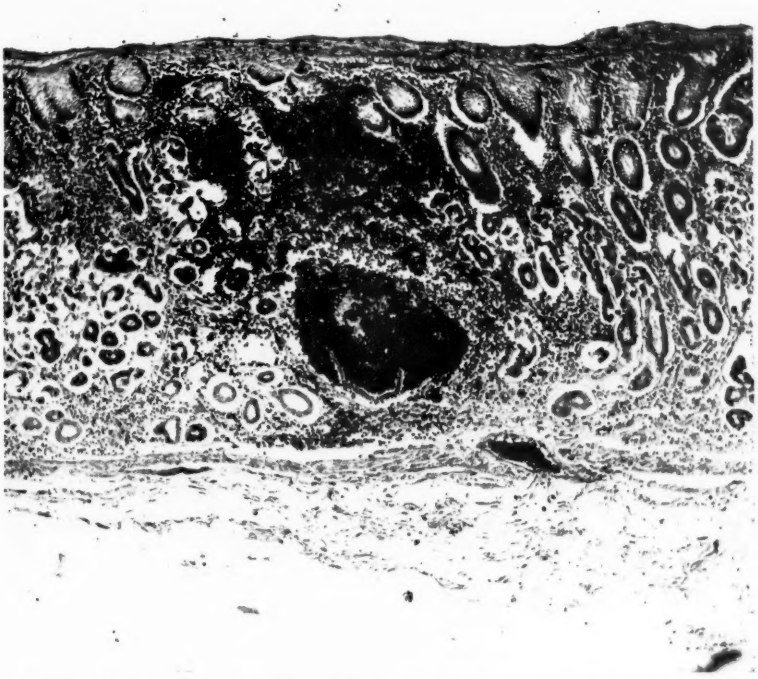

Fig. 11. Case 5. Type of antemortem mucosal hæmorrhage associated in other areas with erosions (mag. × 75).

and the heart was slightly enlarged. Occasional hyaline casts were found in the urine and on two occasions the slightest possible trace of albumin. The examination was otherwise negative.

On *February 5*, to exclude tumor, ventriculograms were made and the ventricular cavities found to be normal in position and outline. On *February 10*, a sudden hæmatemesis occurred with vomiting of 500 cubic centimeters of blood. This was repeated on the following day with the loss of another 800 cubic centimeters of blood. For the resultant secondary anæmia (hæmoglobin 50 per cent, erythrocytes 1,920,000), the patient was treated medically and seemed to be doing well when suddenly at 5 p.m. on *February 17* he was seized with severe epigastric pain, and an exploratory operation by Dr. John Powers disclosed a perforation in the posterior wall of the stomach 1 centimeter in diameter and 8 centimeters proximal to the pylorus. This ulcer was closed, inverted, and plicated, and the patient transfused. He did reasonably well for the next five days when he became comatose and died *February 22* at 7.30 p.m. with a rectal temperature of 104 degrees.

Autopsy (*February 23rd*, 8.15 a.m.) revealed a peritonitis restricted to the lesser peritoneal cavity with terminal septicæmia from a gas-producing bacillus. The sutures closing the perforation had been dissolved away and the stomach was in shreds from autodigestion. The pancreas had become involved and there was extensive fat necrosis. Postmortem changes in the brain, which was riddled with gas bubbles, made its microscopical study unprofitable. Apart from considerable sclerosis of the cerebral vessels, there was no tumor or other observable organic lesion.

In striking contrast were the simple gastric erosions observed at the early autopsy on Case 6 and the extreme autolysis of the stomach found in this last case in which the examination had been delayed for twelve hours. The lesions in both might well enough have been regarded as having been due to postmortem digestion had it not been for the hæmorrhagic nature of the erosions in the first case and the history in the other, of a perforation which occurred five days before death.

The possible dependence of what is known as gastromalacia upon some neurosecretory disturbance in the gastric wall prior to death may next be considered.

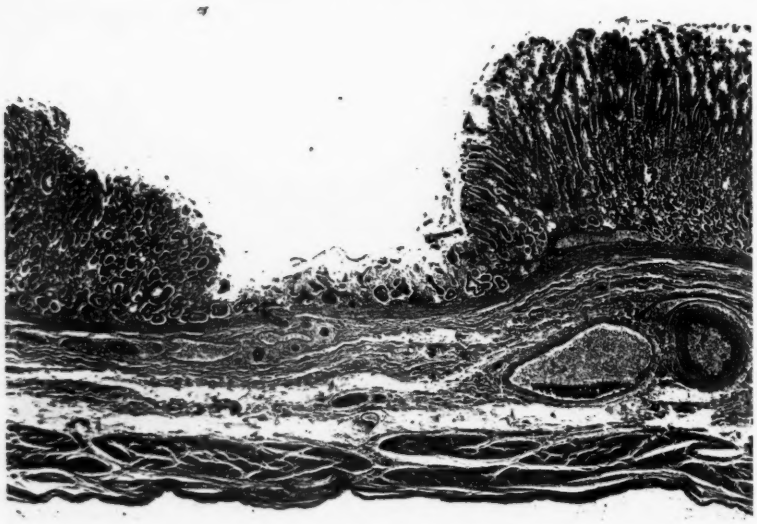

Fig. 12. Case 6. Showing type of erosion associated with thrombosed vessels in submucosa (mag. × 22).

d. Gastromalacia

In his first communication to the Royal Society, made somewhat reluctantly at Sir John Pringle's solicitation, John Hunter stated that after death, a "dissolution of the stomach at its great extremity" is occasionally found; and as this condition had been most frequently seen in the bodies of those who had died violent deaths, it was naturally ascribed to a postmortem continuance of digestion.[1] Why the stomach does not digest itself during life Hunter answered much as the question might be answered today, by saying it can only do so when deprived of the "living principle." Even this was doubted by Claude Bernard and his English pupil, Pavy, of Guy's Hospital who showed that the solvent power of the gastric secretion could act on living tissue. It was assumed that the layer of mucus was what protected the secreting membrane from the action of its own juices, until Pavy in 1868 offered an explanation so simple it met with almost universal approval at the time and in various guises is periodically revived—in effect, that the normally alkaline blood circulating in the stomach walls counteracts the acid of the mucosal secretion.

Death does not commonly occur among hospital patients with chronic maladies while their stomachs are digesting food and this may account for the fact that what is known as gastromalacia, once the subject of ardent discussion, is nowadays infrequently seen and rarely mentioned. While something more will be said of this matter later on, two examples of the process may here be cited as an extreme contrast to the minute erosions described in Cases 4, 5, and 6 and the acute perforative lesions in the first three cases recorded.

[1] Years later, another Scot, Robert Carswell (*cf.* Edinb. M. & S. J., 1830, xxxiv, 282–311), putting this to the test of experiment showed: (1) that the dependent portion of the stomach of rabbits killed after feeding was always found digested; (2) that the gastric juice from such an animal transferred to the empty stomach of a dead rabbit would digest its wall; and (3) that autodigestion did not occur in the stomach of an animal killed while starving, or in one whose gastric contents were immediately washed out after death. In short, postmortem autodigestion only occurs when the stomach is secreting. It remained for Pavlov and others to make clear that the presence of food in the stomach was not the only factor in exciting the flow of gastric juice.

Case 8. (Surgical No. 25562.) *Symptoms suggesting a right cerebellopontile tumor. Negative exploration. Fatality on third day. Autopsy: Large aneurism of basilar artery; extreme œsophago-gastromalacia.*

Archibald McL., a mining engineer aged 47 years, referred from the Battle Creek Sanitarium, was admitted *January 11, 1926*, for a presumptive cerebellar tumor.

Anamnesis. There had been: (1) for seven years, suboccipital headaches produced by any sudden jar and progressively increasing in severity; (2) for four years, a continuous bilateral tinnitus, deglutitory difficulties, a sensation of tightness in the right face, and diplopia on looking to the left; (3) for one year, ataxia of hands and a drunken instability of gait; (4) for two or three months, a right facial palsy, constipation and difficulty of emptying the bladder.

Examination. This disclosed a low grade of papilledema, nystagmus, a right trigeminal hypæsthesia, paresis of the right face, a moderate bilateral deafness, ataxia of cerebellar type, and an absent gag reflex

with some dysphagia and dysarthria. The blood Wassermann was negative; the blood pressure 140/80. A tumor of the right lateral recess was predicted.

Operation: January 26. A suboccipital exploration under local anæsthesia failed to reveal the expected tumor. The manipulations, while in search of it, produced a marked fall in blood pressure and provoked spells of vomiting which continued off and on during the remainder of the procedure. There was no herniation of the cerebellar tonsils; in fact, the upper spinal cord appeared to "ride" higher in the foramen than usual, the ninth, tenth, and eleventh nerves being well exposed to view. The wound was closed.

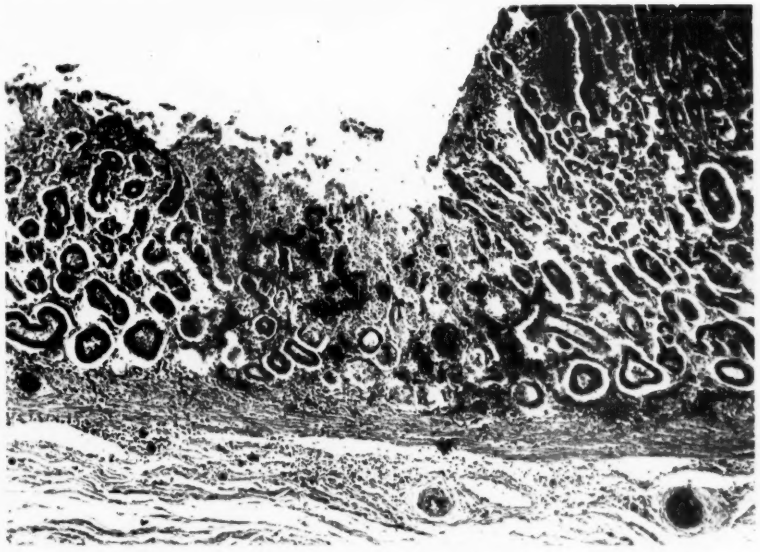

Fig. 13. Case 6. Showing congestion and thrombosis of mucosal veins with beginning erosion. Note constricted and thrombosed artery in lower right hand corner of field (mag. × 80).

During the remainder of the day he vomited frequently and for some unaccountable reason his dysphagia and dysarthria were more marked than before. On the following day, *January 27*, though still nauseated his condition was good and no anxiety was felt regarding his recovery. On the morning of *January 29*, the third day, he seemed to be doing well but he was found at noon to have a temperature of 104 degrees. A lumbar puncture was performed disclosing faintly blood tinged fluid under no increase of tension. During the afternoon, the lungs began to fill with secretion, he became increasingly cyanotic, and passed into a deep stupor followed by death at 1.30 a.m. on *January 30*, the morning of the fourth day. Because of deglutitory impairment no nourishment had been taken by mouth for over 12 hours.

Autopsy: 7.30 a.m., six hours after death (Dr. H. Pinkerton). This disclosed: (1) a large aneurism of the basilar artery greatly distorting the brain stem (Fig. 14); (2) generalized arteriosclerosis; (3) a terminal bronchopneumonia; and (4) gastromalacia. The peritoneal cavity in the region of the spleen contained 500 cubic centimeters of brownish dirty fluid containing small masses of mucus. The fundus of the stomach and lower œsophagus were found to be completely disrupted and in shreds. A perforation measuring 15 centimeters in diameter was present with dissolution of the adjacent stomach wall. The rupture extended up to the cardia and into the œsophagus for a distance of about 10 centimeters. The pyloric region showed considerable autodigestion which involved the superficial layers only.

Here was a typical example of postmortem autolysis of the stomach and œsophagus in which the presence of changed blood in the gastric contents was not observed during life. But inasmuch as no nourishment had been taken, the presence of half a litre of brownish fluid found free in the abdomen can scarcely be accounted for unless the gastric mucosa had been actively secreting long before the cessation of circulation.

In the following example of gastromalacia, evidences that erosions were present before death are somewhat more definite.

Case 9. (Surgical No. 34711.) *Extirpation of right parietal metastatic hypernephroma. Death after 36 hours. Antemortem regurgitation of blood containing fluid. Autopsy: gastromalacia and œsophageal perforations.*

John G., a carpenter, 58 years of age, was admitted *August 28, 1929*, in a stuporous condition with the history of headaches for the preceding six months. The eyegrounds were normal; there was no evidence of nephritis or arteriosclerosis. In the process of making a ventriculogram for diagnostic

Fig. 14. Case 8. Aneurism of the basilar artery (nat. size) mistaken for tumor of right lateral recess (*cf.* projection of sac to left) and causing marked deformation of brain stem.

purposes the needle entered a xanthochromic cyst in the right parietal lobe.

On *September 10th* (9 a.m.), an exploratory operation under novocain was made by Dr. Horrax and a partly cystic tumor which proved to be a metastatic hypernephroma was enucleated. On the following day at 10.30 a.m. because of continued stupor and a rising temperature (104 degrees) the flap was re-elevated under the mistaken belief that a postoperative clot had formed.

The patient remained unconscious and unresponsive with stertorous respirations and an evident hemiplegia. At 6.30 p.m. he was given a nasal feeding which was promptly regurgitated with a large amount of dark brownish material evidently containing changed blood. Death occurred at 9.45 p.m., eleven hours after the second operation with a rectal temperature of 103.4 degrees.

Autopsy: 3 hours after death (Dr. Connor). The brain showed œdema of the right cerebral hemisphere but contained no additional metastases. There was a primary hypernephroma of the left kidney and bronchopneumonia. A bilateral perforation of the œsophageal wall communicated with the right and left pleural cavities, each of which contained about 400 cubic centimeters of brownish mucoid fluid containing fat droplets. The œsophageal openings measured from 4 to 5 centimeters in length, and the adjacent œsophageal tube was necrotic, only a few strands of fibrous tissue, nerves, and blood vessels remaining. The margin of the digested area in the thorax showed a border of reddening suggesting that the circulation must have been in action at least in the early stages of the process. The fundus of the stomach was highly necrotic, with only a few blood vessels, nerves, and strings of reddish mucous material

remaining. The pyloric end of the stomach was comparatively unaffected and the remainder of the gastro-intestinal tract showed no change.

The important features of this example of œsophago-gastromalacia from the point of view of the present discussion are: (1) the presence of dark-brown fluid (probably blood-containing) regurgitated three hours before death; (2) the note in the pathologist's protocol that the appearance suggested an antemortem even if an agonal process. As in Case 3, also with œsophageal perforation, it is difficult to understand how the pleural cavity should have contained such a large amount of blood-containing gastric fluid had the stomach not been actively secreting and have retained its motility after the perforations occurred even were they agonal events. As this is the only tenable explanation for the conditions found, it presupposes some disturbance of control on the part of the vegetative nervous system which served in some way to set aside Hunter's "living principle" and at the same time to provide an abundant gastric secretion. For in the absence of active gastric juice the process could hardly have occurred.

e. Chronic Ulcer

All the lesions discussed up to this point might well enough have been ascribed to postmortem or agonal changes had it not been for symptomatic evidences of peritonitis or of pain or of blood in the gastric contents several hours before death. Even so, the process in all instances has been an acute one whereas the cardinal clinical feature of a gastric ulcer is its peculiar chronicity. This, first clearly pointed out by Cruveilhier, must have been known to John Hunter, to judge from Clift's drawings of some of his specimens published in Matthew Baillie's *Morbid Anatomy* (1799); but just what Hunter thought about them, unfortunately, went up in smoke when his manuscripts were burned.

What it is that favors chronicity in a gastric or duodenal ulcer is a much debated subject. All will agree, however, that an erosion of the mucosa must be the primary stage in its formation; and since there is every reason to believe that acute erosions (of the type described in Case 5) are of common occurrence, any one of them may well enough be the precursor of a chronic lesion, should the original insult be sufficiently great or should a minor insult be continuous or frequently repeated at the same spot. As a matter of fact, a duodenal ulcer at least shows every inclination to heal, as indicated by the frequency with which shallow scars are found after death, and its tendency to recur, rather than any pathological evidence of chronicity, is its peculiar characteristic.

Only one pathologically verified chronic ulcer which, with reasonable assurance, can be ascribed to an encephalic lesion, has been observed in our tumor series. The history of the case follows:

CASE 10. (Surgical No. 29708.) *Radical removal from a child of a median cerebellar medulloblastoma with wide opening of fourth ventricle. Repeated subsequent radiotherapeutic sessions. Death after two years. Massive intraventricular recurrence. Duodenal ulcer with evidences of cicatrization.*

The patient, Ruth F.,[1] aged 9, was admitted September 23, 1927, with an advanced cerebellar tumor syndrome of seven months' duration: headaches, projectile vomiting, loss of weight, anorexia, cerebellar ataxia, and choked discs.

At operation on *October 6, 1927*, a typical midline cerebellar medulloblastoma was cleanly extirpated, chiefly by suction, leaving the floor of the fourth ventricle fully exposed. The patient made a good recovery from this operation and was subsequently given X-ray treatments over the entire cerebrospinal axis at intervals of from two to four months. For the first year she remained wholly free from symptoms.

She was readmitted to hospital *July 29, 1929*, because of the abrupt accession of symptoms of a week's duration. A series of six X-ray treatments were then given and she was again discharged. For the first time, no improvement followed this series of radiations and on *September 21, 1929*, she was again admitted to hospital. She had become apathetic, incontinent, and emaciated. There were daily attacks of vomiting; feeding was a difficult problem; there was a constant slight pyrexia.

In spite of her desperately poor condition, a reexploration of the cerebellar region was made on *October 10*. This was disappointing in that it failed to disclose the expected local recurrence, the fragment of tissue that was removed after redividing the vermis proving, under supravital preparation, to be wholly degenerated tumor. In the course of the operation clear fluid had been obtained by a puncture of the cerebral ventricles, and this, on examination, failed to show any tumor cells.

[1] Case 50 of medulloblastoma series as reported: Acta Path. et Microbiol., Scand., 1930, vii, 1-86.

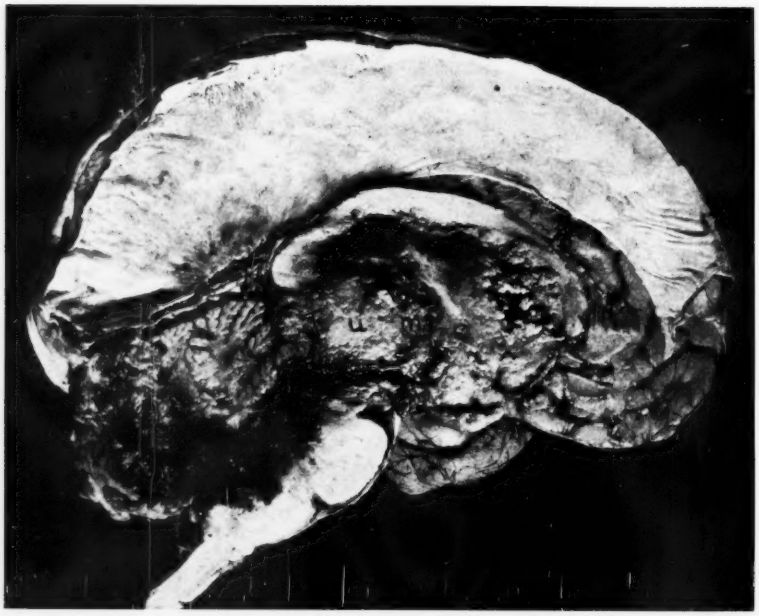

Fig. 15. Case 10. Note invasion of medulla and massive obliteration of cerebral ventricular system by recurrent medulloblastoma.

Following this futile procedure, the child's critical condition remained unchanged. In the subsequent bedside notes, attention was called to her abundant perspiration which was limited almost wholly to the right side of the face. She gradually passed into coma and died on *October 27* at 2.42 p.m., with a terminal hyperthermia (106.5 degrees). An unrestricted post-mortem examination was held one hour later.

Autopsy: 3.45 p.m. (Dr. Schulz). Two striking things were disclosed: (1) a massive intraventricular involvement by tumor (Fig. 15) in the absence of macroscopical evidence of tumor implantation in the spinal or cerebral meninges; and (2) a chronic duodenal ulcer. The œsophagus and stomach were wholly normal in appearance, the mucosa being well preserved, but in the first portion of the duodenum, 3 centimeters below the pyloric sphincter, was a small ulcer measuring 3 by 4 millimeters. It had a firm, elevated margin and depressed center forming a crater. The lower bowel elsewhere was apparently normal.

Microscopical examination of the ulcer shows that it extends down to the muscularis, that its margins are steep and slightly undermined (Fig. 16). On its floor there is a narrow zone of dense hyalinized connective tissue, and in one region some fibrin and blood cells. Within the excavated crater lie desquamated epithelium and blood elements. The scar tissue at the rim of the ulcer shows chronic inflammatory cell infiltration. In the adjacent tissue are small thrombosed blood vessels filled with fibrin and a few polymorphonuclear leucocytes (Fig. 17).

In this case a large recurrent, thoroughly radiated medulloblastoma filled the cerebral intraventricular system. The child had been subject to frequent attacks of sudden vomiting, but as this is characteristic of most cerebellar tumors, its possible association with a peptic ulcer was not suspected, nor were any studies made in this direction. During the course of cerebellar operations on patients under local anæsthesia, it is well known that vomiting may be easily provoked, and this is commonly ascribed to stimulation of the vagal nucleus in the floor of the fourth ventricle. What is more, all neurosurgeons are familiar with the fact that after major intracranial operations the vomitus for the first few days may show evidences of changed blood. While this is usually attributed to the swallowing of blood from some source during the progress of the operation, it is highly probable that it may be due, more often than is commonly supposed, to acute neurogenic erosions.

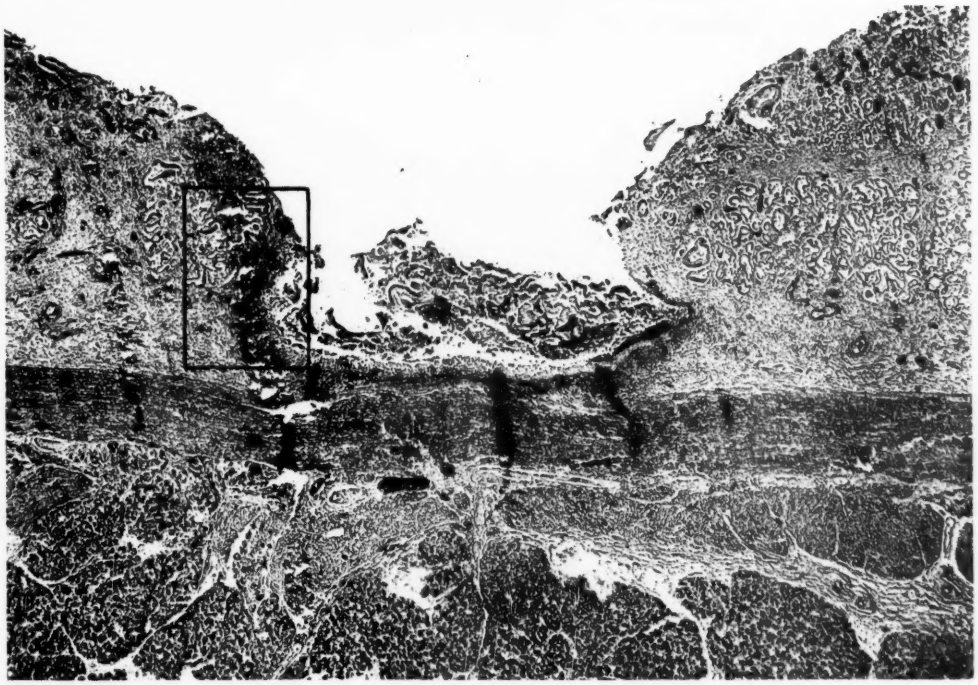

Fig. 16. Case 10. Showing duodenal ulcer (mag. × 20) in child associated with tumor metastasis involving third ventricle (*cf.* Fig. 15).

Though I am not aware of any other examples in my tumor series of the postmortem finding of a chronic ulcer, we not infrequently see in the hospital wards patients recovering from serious intracranial operations in whom during convalescence digestive disturbances are in evidence which strongly suggest incipient ulcer symptoms. But this perhaps is true no less of operations of other sorts. Somewhat more definite is the fact that a goodly number of patients with symptomatic evidences of an organic lesion in the region of the third ventricle have had a roentgenologically demonstrable gastric or duodenal ulcer. The following example will serve in illustration.

CASE 11. (Surgical No. 34129.) *Tumor of third ventricle (demonstrated by ventriculography) causing pressure symptoms associated with gastro-intestinal disturbances. Subsequent periodic radiation of lesion with marked improvement. Recurrent duodenal ulcer.*

Edward C., an electrician, aged 25 years, was admitted *June 5, 1929*. Apart from periodic indigestion, to which scant attention was paid, he had enjoyed uniformly good health. Suddenly, on *May 12, 1929*, fatigued by a 200 mile motor car drive, he had a sudden severe occipital headache with vomiting. A succession of these occurrences followed and he was soon obliged to give up work. The seizures which came in paroxysms were characterized by retraction of the neck, dizziness, sweating, protrusion of the eyes, and painful flexure of the arms; they would terminate with a cough or a yawn when sudden relief would be experienced. He was taken to a hospital on *May 31* and treated for "gastric symptoms." While under observation, he acquired a diplopia with choked disc and was transferred to the Brigham Hospital as a brain tumor suspect.

Examination. This showed a man with a rigid neck, a bilateral abducens palsy more marked on the right, and a choked disc of 4 diopters. The reflexes were hyperactive, with a bilateral Babinski. Ventriculograms disclosed a symmetrically disposed hydrocephalus with a filling defect of the third ventricle and a block of the foramina of Monro. He was given a series of four X-ray treatments, began promptly to improve, and the choked discs rapidly subsided. He was discharged *June 23* practically symptom-free and two weeks later resumed his occupation.

Fig. 17. Case 10. Showing, from squared area in Figure 16, thrombosed vessels and cicatrization of mucosa in lower right part of field (mag. × 100).

He remained well for over a year when he once more began to have "nervous indigestion" associated with nausea and hunger pains for which he finally reported to the ambulatory clinic. Suspecting that these symptoms might be due to a recurrence of the intracranial lesion, and as the patient was unwilling to re-enter the hospital for study, the attendant recommended further radiation of the third ventricle and on *February 18, 19, and 21, 1931*, three additional treatments were given. After an interval of two weeks, the symptoms again disappeared and he was lost sight of. No dietary restrictions had at any time been imposed.

Eleven months elapsed when on *January 18, 1932*, he again reported to the clinic stating that his gastric symptoms had recurred and he wished to have more X-ray treatments. Because the symptoms were so suggestive of ulcer, barium studies were made and a typical active duodenal ulcer was disclosed. As he was unwilling to enter the hospital to have his ventriculograms repeated, he was given another series of radiotherapeutic treatments on *January 18, 19, 20, and 21*, directed to the third ventricle. Within three days after the last session, the symptoms of indigestion had wholly disappeared and he returned to work. He reported on request, *March 3*, for barium studies which showed the trace of a healed ulcer unassociated with local tenderness. He was symptom free and could eat the most indigestible articles (*e.g.* cabbage) without discomfort.

Here, then, was a symptomatic and roentgenologically demonstrable duodenal ulcer associated with a symptomatic and roentgenologically demonstrated tumor of the third ventricle. The growth fortunately proved to be susceptible to the effects of roentgen therapy, and when pressure symptoms were thereby relieved the gastric symptoms promptly subsided. Indeed, in the absence of any actual return of intracranial symptoms, therapeutic radiations of the third ventricle have on two subsequent occasions had a prompt and long enduring effect in checking the recurrent symptoms of the ulcer.

Other examples of symptomatic and roentgenologically demonstrable ulcer have been encountered in association with diabetes insipidus and with tumors of the nervus acusticus; but it is needless further to pile up the evidence drawn from a single clinic, particularly since the relation of organic intracranial disease to peptic erosions or ulcers will come up for later discussion.

II. PATHOGENESIS OF PEPTIC ULCERATIONS

A satisfactory, all-embracing explanation of acute or chronic ulcerations of stomach and duodenum is yet to be found. From the first it has been a highly controversial subject regarding which there are many divergent views. Until an acceptable explanation is reached, we cannot look forward to the prevention of ulcer, and physicians and surgeons will continue to differ widely in their views regarding the proper therapeutic regimen to follow in its active stage and how to forestall its tendency to recur when once healed. What is more, even those surgeons who believe that most ulcers should be operated upon differ in the procedures which they advocate for its

cure or alleviation. It, indeed, is doubted in some quarters whether hæmorrhagic erosions (*cf.* Cases 4 and 5) or acute perforative lesions (*cf.* Cases 1, 2, 3, and 7) or gastromalacia (*cf.* Cases 8 and 9) are in any way related to chronic ulcer, it being the fashion just now in some foreign clinics to ascribe ulcer, as Cruveilhier did long ago, to an antecedent gastritis.

The literature of ulcer pathogenesis is enormous. In his review of the subject [6] in 1911, Moeller cited 325 references, and this number in the intervening two decades has probably been quadrupled. Based on experiment or on experience at bedside and operating table, pathologists, physiologists, pharmacologists, and clinicians have offered innumerable explanations. Old hypotheses long forgotten are from time to time revived with some slight modification, and the fact that in defence of each one of them a strong brief could be written means that in all probability more than one causative element must be concerned. It indeed is quite possible that the several hypotheses—vascular, traumatic, secretory, toxic, bacterial, biochemical, and so on—are capable of being harmonized.

Most of the attempts experimentally to produce in the lower animals peptic ulcers have been made on the stomach itself under the assumption that the disorder is essentially a local one. Erosions and occasionally chronic ulcers have thus been produced by a great variety of procedures which in most instances are remote from the circumstances in which ulcer so commonly occurs in man. Attention, indeed, has been so largely confined to the local search for an explanation of the lesions that their ease of production by injuries of the central nervous system has been largely forgotten though it is an old story. In his discussion of ulcer pathogenesis in 1885, Professor Welch stated [7] that "the neurotic theory of the origin of gastric ulcer is altogether speculative and has never gained wide acceptance." While this view is generally held at the present day, the evidence in favor of the theory is nevertheless accumulating and in the succeeding sections I shall endeavor to draw it together as briefly as circumstances make possible.

a. Neurogenic versus local Explanations

In a section of his celebrated *Handbuch der pathologischen Anatomie* (1841–1846)[1] dealing with "the ulcerative processes of the stomach," Carl Rokitansky described with unsurpassed clearness, brevity, and detail all the processes that have been illustrated in the eleven cases given above—acute perforating ulcers, hæmorrhagic erosions and the simple chronic ulcer. He also described two forms of acute softening which he sharply distinguished from cadaveric softening or self-digestion of the stomach. The first of them, a gelatinous softening, occurs in the newborn and is frequently associated with a demonstrable intracranial lesion; hence, "the proximate cause may be looked for in diseased innervation of the stomach, owing to a morbid condition of the vagus, and to extreme acidification of the gastric juice." Of the second form of softening he distinguishes two types: one of them "occurs, both in children and adults, as the sequel of acute affections of the brain or its membranes, and is probably brought about by a reflex action of the œsophageal and gastric branches of the vagus"; in the other type associated with cachectic states, the stomach contains large quantities of "coffee-ground" fluid which is often vomited during life. Softening of this latter type often attacks the lower third of the œsophagus (*cf.* Case 3) leading to perforation and effusion into the left thorax. He admits that a conscientious pathologist may find difficulty in distinguishing between cadaveric softening and morbid softening unless he take the clinical history and mode of death into consideration.

This, so far as I can gather, is the first definite suggestion that any of the ulcerative processes under discussion may have a neurogenic origin. So far as chronic ulcer is concerned, Rokitansky does not go further than to state that it probably commences as an acute circumscribed hæmorrhagic erosion which increases by sloughing and exfoliation layer by layer, and is invariably accompanied by a chronic catarrh of the mucous membrane.

Though his works are no longer read and his reputation as a pathologist was soon to be

[1] The third volume, in which the pathology of the organs of nutrition is considered, was the first to be published (1841).

eclipsed by the greater fame of Virchow, Rokitansky's teaching based on a vast experience gained at the autopsy table made a deep impression on his contemporaries which still endures. Thus, for example, there survives in Vienna, whence it has spread into many pathological laboratories throughout the world, a tradition of the deadhouse, in effect, that autolytic destruction of the stomach is most often found in the bodies of persons who while digesting have died from an intracranial disorder, particularly when it was associated with a terminal fever of high degree. Beyond this the general subject of gastric erosions or of gastromalacia arouses no present-day interest and is scarcely mentioned in contemporary textbooks on pathology. That it has any possible bearing upon or any possible relation to chronic peptic ulcer is no longer even suggested.

Traceable to Virchow is the concept that ulcer is essentially a local process; and out of this has come the highly unprofitable search for its primary cause in the walls of the stomach itself—a search beset by pitfalls and contradictions. The discredited view of Rokitansky, on the other hand, that the disorder has a neurogenic source has slowly but surely gained ground[1] as our knowledge of the vegetative nervous system and its cerebral connections has increased. His influence may be traced in four more or less independent directions which deserve separate consideration. The *first* of them leads to the association of brain tumor and ulcer in regard to which, so far as I can observe, he made no allusion; the *second* concerns the gastroduodenal ulcers and erosions of infancy; the *third* leads to the experimental production of ulcer by lesions of the nervous system; and the *fourth*, to concepts concerning ulcer production which have been looked upon as somewhat fantastic though based securely on pharmacological grounds. The last of these four currents of thought is the most important; but to the others some reference, however brief, may in turn first be made.

[1]In his brief discussion of ulcer in the article usually quoted (Virchow's Arch., 1853, v, p. 363), Virchow makes no reference to Rokitansky and merely refers to a recent article by Guensburg (Arch. f. physiol. Heilk., 1852, xi, 516–527) who on the basis of a single clinical case showing hyperacidity advanced views regarding the possible vagal influence on ulcer similar to those which Rokitansky had propounded eleven years before. It is probably because of this that Guensburg's paper is so frequently referred to, as, for example, by Ewald in his "Lectures on Diseases of the Digestive Organs" (New Sydenham Society, London, 1892, ii, 425 *et seq.*) who quotes Guensburg as saying that "the [ulcerative] destruction of the mucous membrane of the stomach proceeds from a quantitative anomaly of the secretion of free acids."

b. Ulcers and Intracranial Disorders

In most of the eleven cases assembled to illustrate this report, the surgical procedure and not the tumor was looked upon as the provocative cause of the lesions in the upper alimentary canal. The exceptions were the two cases of hypertension with choked disc (Cases 6 and 7), the man (Case 11) with an unverified tumor of the third ventricle, and the child (Case 10) with intraventricular metastasis. As a matter of fact, in the absence of operative intervention, acute or chronic ulcers are known to accompany intracranial tumors, when properly situated to produce them, more often than can be explained by mere coincidence. The remarkable thing is that the combination of the two lesions should occur at all and be found postmortem, for an acute perforative gastric lesion is so obviously the immediate cause of death the brain may not be examined; or should an obvious intracranial tumor lead to a fatal issue, permission for a postmortem examination is likely to be restricted to an examination of the brain alone.

Not only, therefore, are the combined lesions—brain tumor and ulcer—unlikely to be observed, one masking the other, but, what is more, when observed and reported they are not easily located. Nevertheless, a few examples, old and recent, may be given. In 1868, Professor Carl Hoffmann, of Basel [8], one of the early upholders of the view that softening (œsophago- or gastromalacia) was a process which began before death, described two cases of œsophageal perforation in adults with antemortem signs of peritonitis. The second case had definite intracranial symptoms and was found at autopsy, three and a half hours after death, to have a gummatous, interpeduncular tumor with softening of the right half of pons and medulla.

In 1874, Rudolf Arndt, the Greifswald psychiatrist, in illustration of the fact that functional disturbances may produce symptoms remote from the seat of organic disease, reported the case [9] of a 26 year old woman

with nutritional disturbances, somnolence, amenorrhœa and vomiting, who died from the effects of a walnut-sized sarcoma of the meninges occupying the interpeduncular space at the base of the brain. There was also disclosed, during the examination, a hyperæmic softening of the stomach with numerous ecchymoses of the fundus, a condition which was ascribed to a reflex disturbance of vagal innervation. Aware that this was not a very convincing case, some years later Arndt reported another example [10]—that of a man of 55 with cerebellar symptoms and Cheyne-Stokes respiration who was found after death to have a median cerebellar tumor compressing the corpora quadrigemina and medulla together with a markedly hyperæmic and ecchymotic lower œsophagus and duodenum in association with ecchymoses, extravasations, and hæmorrhagic erosions of stomach. On the basis of these findings, and of the experiments of Schiff and of Ebstein to be referred to later on, the author suggests that round ulcer is an angioneurosis or trophoneurosis, the acute erosions being regarded, in agreement with Rokitansky, as an early stage of the chronic form of ulcer.

Scattered through medical literature under various titles may be found other examples. In a study of the source of postoperative hæmatemesis observed in von Eiselsberg's clinic after surgical operations, von Winiwarter [11] stated (1911) that in two unaccountable instances fatal bleeding from the stomach had followed intracranial operations; and in view of my own experiences it is curious that both of them were suboccipital operations for supposed cerebellar tumors.

Subsequently, pathologists in various university centers began to show a renewed interest in these matters. Thus, in 1908 [4] Professor Beneke of Marburg, in a study of the causes of "black vomit," furnished statistics concerning gastric erosions and ecchymoses observed in 293 autopsies on medical cases; and though the statistics are somewhat difficult to appraise, the two largest single groups accompanied by erosions were represented (1) by diseases involving organs adjacent to the stomach, and (2) by a group of sixty intracranial disorders, to which ten others classified as "shock in the newly born" might well be added. In 1910 Professor Roessle of Jena made the interesting suggestion [12] that ulcer was commonly a secondary disease (*zweite Krankheit*), reflexly produced through irritation of the vagus by a primary disease elsewhere. Acting upon this idea, in 1918 Professor Carl Hart, of Berlin [13], attempted to determine the relation, if any, between peptic ulcer and remote disorders; and he found to his surprise that 17 per cent of the ulcers disclosed postmortem during a period of four years were associated with affections of the brain—a percentage exceeding that in which cardiovascular disorders, tuberculosis, or cholelithiasis represented the "*erste Krankheit*."

Still more important have been certain studies emanating from the University of Moscow, where, under the leadership of the pathologist, Mogilnitzky, particular attention has been paid to the relation to ulcers of intracranial lesions definitely affecting the interbrain, more particularly the corpus Luysii. In 1925 [14] he briefly mentioned four examples of fatal intracranial disorders associated with gastric ulcer; and three years later his pupil, Korst [15], after mentioning that Mogilnitzky had observed eight cases of tumor of the mid- or inter-brain with gastric or duodenal ulcer proceeds to give three other highly interesting examples. One of them was a frontal lobe tumor involving the basal ganglia in which degenerative processes were observed in the right hypothalamic nucleus on the corresponding side; the second case, a three year old child, had an ependymal tumor of the fourth ventricle which had compressed the vagal nucleus and caused a marked hydrocephalus, all the vegetative nuclei of the third ventricle being found degenerated; the third case was one of hydrocephalus associated with sclerosis of the brainstem and a complicating meningitis. In all three instances hæmorrhagic erosions of the gastric mucous membrane were found after death.

c. Ulcerative Processes in Infancy

Five years after Rokitansky's observations were published, there appeared a monograph [16] by Elsaesser on autodigestion of the

stomach as it occurs in the newborn; and this much quoted article served to revive the polemics between representatives of the Berlin and Vienna schools as to whether the process was purely cadaveric or whether it started *intra vitam*. Elsaesser's report was based on the study of thirty-eight examples which he had observed, many of them having been found in association with intracranial disorders; but he emphasizes that erosions and softening occur only when the stomach is actively digesting at the time of death. Though the postmortem examinations in all instances were delayed for twenty-four hours or longer, autodigestion was never observed except under the conditions mentioned.

The bearing of all this upon the erosions, perforations, and ulcers of the newly born, often associated with melæna neonatorum, appears to be very largely overlooked or forgotten, due possibly to the fact that immediately after parturition the mother gets more attention than the child. There nevertheless has been a later-day revival of interest in the subject. In 1911 it was pointed out by Rudolf Pott [17] from Beneke's laboratory in Halle that intracranial birth hæmorrhages are usually caused by lacerations of the dura near the junction of tentorium and falx resulting in extravasations of blood into the posterior fossa.

In several of the many reported cases, hæmorrhagic mucosal erosions and occasionally hæmorrhages into the adrenal glands were described in the autopsy protocols without any comment on their significance. In 1892, however, the attention of Professor v. Preuschen of Greifswald was drawn to the matter by the example of an infant with melæna who died on the second day after birth, the autopsy showing (1) a subtentorial hæmorrhage with extravasation into the fourth ventricle, and (2) hæmorrhagic erosions of the gastric mucosa [18 . He was led to believe that an intracranial lesion might be a common cause of melæna in infants, and in collaboration with Pomorski, then an assistant in Grawitz' laboratory [19], experimental injuries of the hind brain were made in animals demonstrating the fact that erosions of the gastric mucosa were common sequels of such lesions.

Though the examples of gastromalacia described by Elsaesser and the erosions of v. Preuschen mentioned above have been acute lesions, ulcerations of more chronic type which occur in the duodenum of infants and which are roentgenologically demonstrable, have more recently been the object of attention. Emmett Holt, in 1913, made a careful study of the subject [20] and two years later Gerdine and Helmholz [21] recorded a series of eleven infants who before death had shown blood in vomitus or stools, duodenal ulcerations occasionally with perforations having been found at autopsy in all instances. Whereas v. Preuschen after due consideration discarded as improbable the bacterial origin of ulcer in the newly born, Gerdine and Helmholz warmly supported their colleague Rosenow's well known views in this regard, all of the lesions which were histologically examined having shown diplococci or streptococci. Attention, however, may be drawn to the fact that in the only three instances in which the brain was examined meningitis was the cause of death; and it may also be noted that streptococci and staphylococci are organisms normally found in the upper part of the alimentary canal.

In the series of cases that I have reported, only three were children, one of whom was found to have had a perforation of the œsophagus. When this was called to the attention of my colleague, Professor K. D. Blackfan, he kindly looked into the matter and somewhat to his surprise, I believe, found in the autopsy series for 1931 at the Children's Hospital in Boston four examples of death from œsophageal perforation associated in all instances with an intracranial lesion (occlusion of the aqueduct of Sylvius with hydrocephalus 1, meningitis 3). In all instances vomiting had characterized the malady and in one at least it contained large amounts of changed blood.

In his *Textbook of Diseases of the New Born* (page 448), Von Reuss states that melæna occurs more frequently after prolonged and difficult labors and suggests that cerebral birth injuries may predispose to erosions; and it is, of course, well known, as Helmholz and others have pointed out, that the roentgeno-

logically demonstrable duodenal ulcers in infants and children are prone to heal and probably therefore are often overlooked.[1]

d. Experimental Neurogenic Ulcerations

So far, the argument favoring the neurogenic production of erosions and ulcers may appear somewhat lame, based as it has been: (1) on the lesions which have been seen to occur as a sequel to certain intracranial operations; (2) on the occasional accompaniment of intracranial tumors and ulcers; and (3) on the occurrence of ulcerative processes in the newborn in association with cerebral birth injuries or intracranial disorders of other kinds. The issue has been largely a difference of opinion over the question, on the one hand, whether the erosions and softenings were in any way related to chronic ulcer, and, on the other, whether they were wholly cadaveric lesions or were attributable to processes which were already under way at the time of death. We now come to something more definite, namely, the consequence of experimental lesions; and it may be best to consider separately: (1) *the effect of lesions of the peripheral nerves to the stomach* and (2) *the effect of lesions of the brain.*

1. Peripheral lesions of vegetative nerves. Rokitansky, as has been told, assumed that the intracranial disorders to which he attributed ulcer acted in some way through the mediation of the vagus and this naturally led at many hands to a vast amount of experimental work with highly contradictory results. What is more, reports were made from time to time of gastric ulcers in association with an involvement of the vagus by some pathological process such as a tuberculous lymph node or mediastinal tumor. It has been found in laboratory animals that erosions, at least, may be produced in rabbits or dogs either by stimulating or dividing one or both vagi, whether above or below the diaphragm; and not only this but the same effects appear to follow stimulation or resection of the splanchnic nerves or cœliac plexus whence pass the sympathetic nerves to the stomach.

On wading through the literature of the subject, no possible order would seem to come from this chaos. But if the elementary fact is borne in mind that the thoraco-lumbar (sympathico-adrenal) system of Gaskell and the cranio-sacral (autonomic) system of Langley represent, as Hans Meyer has shown, a nicely balanced dual mechanism, the visceral effects of the two systems being antagonistic one to the other, it becomes apparent, in spite of the many contradictions, that the peripheral lesions which have led with the greatest constancy in the laboratory to ulcerative lesions have either been paralytic on the part of sympathetic nerves or stimulatory on the part of the vagus.

Most of the experimental procedures, naturally enough, because of their greater ease of production, have been paralytic in nature; and though vagal section whether above or below the diaphragm has led to erosions and acute ulcerations at many hands, it is possible that, in the process of paralyzing the nerves, a primary stimulatory effect may actually have been produced. But however this may be, more consistently successful results have followed severance of the splanchnic nerves or extirpation of the cœliac plexus—[*e.g.*, dalla Vedova, 1900 (22); Durante, 1916 (23); and Gundelfinger, 1918 (24)], or from bilateral adrenalectomy [*e.g.*, Finzi, 1913 (25), Gibelli, 1909 (26), and Mann, 1916 (27)].

The effects of long continued peripheral nerve excitation are far less easily investigated. Nevertheless, successful attempts have been made in this direction. Thus, Keppich in 1921 [28] produced gastric ulcers showing definite tendency to chronicity in ten out of eleven rabbits by placing electrodes on the vagi near the cardia and leading them out over the animal's back so that the nerves could be intermittently stimulated over periods from five to twenty-five days. And more recently Stahnke in 1924 [29], avoiding the complicating effects of a primary operation stimulated the vagi in dogs near the cardia by placing his electrodes in the lumen of the

[1] Another condition deserving of mention in this connection as a possible or probable secondary disorder rather than primary anomaly is the so called hypertrophic stenosis of the pylorus in infants. That this may be an expression of hypervagotonus resulting in muscular hypertrophy from spasm rather than a congenital anomaly has been suggested but never given full credence. Prof. Lehmann of Frankfurt a.M. (Ztschr. f. Kinderh., 1931, I, 691–704) has pointed out that it occurs not infrequently in association with megalocolon, cardiospasm, congenital dilatation of the bladder and so on—conditions which may likewise be looked upon as a consequence of hypertonicity in the cranio-sacral autonomic.

lower œsophagus with resultant hypermotility, hypersecretion, pylorospasm, chronic gastritis and ultimate erosions.

So far as the stomach is concerned, on this working basis of imbalance between sympathetic and parasympathetic systems, it is known that vagal stimulation causes increased motility and secretion, whereas sympathetic stimulation gives reverse effects; and as a natural corollary, vagal paralysis diminishes secretion and motility whereas sympathetic paralysis increases them presumably by releasing the vagus from the check normally exercised by the sympathico-adrenal apparatus against its overaction. On these general principles is based the surgical division of the left branch of the vagus as it passes to the stomach wall—a procedure advocated for ulcer patients showing high pre-operative free acidity with hypermotility, and routinely practised by some surgeons both in this country [30] and abroad with results said to be, at least temporarily, excellent.[1]

2. *Lesions of Vegetative Tracts in the Brain*

In 1845, three years after Rokitansky's views became known, Moritz (Maurice) Schiff, a brilliant and highly original pupil of Magendie's, made the interesting observation [31] that a unilateral cerebral lesion in dogs and rabbits involving optic thalamus and adjacent cerebral peduncle would often lead, after a few days, to softening of the stomach and occasionally to actual perforation. Schiff ascribed this to a patchy (*en plaque*) neuroparalytic hyperæmia of the gastric mucous membrane brought about by injury of the central pathway for vasomotor nerves to the stomach. He subsequently observed also [32] that a unilateral division of the pons or of the medulla as far back as the calamus scriptorius, and also that hemisection of the two upper segments of the spinal cord, would cause the same effect. Whether unilateral division of the cord lower down or injuries of the sympathetic nervous system would produce lesions of the same kind he was unable to determine as the animals failed to survive. Nevertheless, by this ingenious series of experiments, he was able to trace the course of the vasomotor nerves of the stomach (*sic*) from the thalamus to the commencement of the cervical cord. He also observed: (1) that stimulation of the corpora quadrigemina, the cerebral peduncles, the pons, and cerebellar peduncle caused gastric movements comparable to those elicited by vagus stimulation; (2) that these movements were blocked by division of the vagi; and (3) that stimulation of the splanchnics, and more particularly of the cœliac plexus, caused contraction of the vessels of the stomach.

Schiff's final views regarding these matters were published in 1867 in his celebrated "Lectures on the Physiology of Digestion" [33]. In general terms, he recognized that there were vasoconstrictor and vasodilator fibers to the stomach; that the former passed by way of the cœliac plexus, whereas flushing effects were produced by stimulation of fibers in the pneumogastric. It requires little imagination, reading between the lines of his discussion, to foresee the present-day distinction between counterbalancing sympathetic and parasympathetic systems, both of them under the control of higher centers which Claude Bernard located in the medulla but which modern views, as will be seen, tend to place in the hypothalamic nuclei of the interbrain.

Schiff's experimental observations were soon repeated and essentially confirmed by others. In November 1875, Brown-Séquard [34], before the *Société Anatomique*, exhibited the stomach of an animal which had died from the effects of a chronic perforative gastric ulcer produced by an injury (cauterization) of the cerebral cortex. While upholding Schiff's views in general, he distinguishes between softening and hæmorrhagic lesions which latter he found to be a uniform consequence of experimental injuries at the junction of the middle cerebellar peduncle and the pons.

More fully reported were the series of contemporary experiments carried out by Wilhelm Ebstein [35], then director of the Medical Polyclinic in Breslau. By injecting chromic acid he made small unilateral punctate lesions alongside the anterior corpora quadrigemina without injury to the adjacent peduncle, and in nine of twenty-three animals succeeded in

[1] It however has been observed that gastric acidity may return in course of months or years after experimental double vagotomy even when associated with a subtotal gastrectomy, indicating a highly efficient compensatory mechanism (*cf.* Shapiro, P. F., and Berg, B. N.: Proc. Soc. Exper. Biol. & Med., 1932, xxix, 743–745.

producing ulcerative erosions. He also got similar though more delayed effects by unilateral lesions of the thalamus, medulla, and of the upper cervical cord, but found complete transsection of the cord to be without effect on the stomach. He attributed this negative result to the consequent lowering of blood pressure whereas the intracranial lesions, presumably from stimulation of a vasomotor center, elevated the blood pressure leading to submucosal extravasations of blood which permitted the corrosive action of the gastric juice locally to take effect.

Similar experiments were conducted some twenty years later by v. Preuschen and Pomorski [18, 19] as an outcome of their interest in melæna neonatorum. Pulmonary and gastric hæmorrhages were produced by punctate lesions of the crura cerebelli, corpora quadrigemina, pons and floor of the fourth ventricle in rabbits. Their most constant results, however, occurred when chromic acid was injected into the right anterior colliculus, only two failures to get ulcerations after ten hours having been observed in eleven animals with lesions made in this situation.

More recently (1925–1926) the matter has been taken up anew by Prof. Mogilnitzki and his surgical colleague Burdenko of the University of Moscow [36]. With the object of stimulating or paralyzing vegetative nervous centers in the diencephalon, more particularly the corpus Luysii which they assumed to be the pathway for vasodilatation, they made lateral punctures into the hypothalamic region and observed in stomach and duodenum not only hæmorrhagic erosions and perforations but also in some instances chronic cicatricial ulcerations. Thus, from the time of Schiff, unilateral lesions, which in some way have affected not only the presumptive source of vegetative (vagal) impulses in the hypothalamus but the supposed pathway of the fibers from this region backward as far as the medulla and upper cord, have in the hands of several investigators led to ulcerative processes in the stomach or duodenum with fairly consistent regularity.

Most of these experiments, as will have been noted, have been made in rabbits, an animal particularly prone to show gastric erosions under a great variety of circumstances; and what is more, the lesions in most instances have been without evidence of chronicity. A far more telling series of experiments has recently been carried out by Dr. Allen D. Keller, professor of physiology in the University of Alabama, who has kindly permitted me to give the following brief reference to his unpublished observations.

> In a study primarily undertaken to throw light on the heat-regulating mechanisms of the brain stem in cats, bilateral lesions were made in the expectation of freeing the hypothalamus from its connections with the brain stem. From these operations the animals recovered perfectly, showed no appreciable effects of the lesions, and appeared to be entirely normal in all respects. After the expiration of a few days, however, they refused food, had spontaneous vomiting, and died in from four to ten days. Postmortem examinations invariably showed gastric lesions ranging from simple hyperæmic areas to erosions extending through all the layers of the gut, and to punched-out perforating ulcers. The definitely delimited hyperæmic areas were always found at the terminal end of a small artery. The preliminary event, in other words, was a characteristic patch of hyperæmia resulting in a submucosal extravasation visible from both mucosal and peritoneal surfaces, and which was definitely the precursor of the mucosal erosion.

Many of these observations, therefore, which are in line with the original concept of Rokitansky tend to conciliate his views with those of Virchow in explaining how the local vascular lesion on which the gastric secretion acts comes to be brought about through neurogenic influences. None of the recorded cerebral lesions that have served experimentally to produce ulcer, except those of Burdenko and Mogilnitzki, have been made higher than the mid-brain, nor have they been sufficiently circumscribed, in want of knowledge concerning the precise pathway for the vegetative impulses, to permit us to determine whether the effects have been due to stimulation or to paralysis of efferent sympathetic or of parasympathetic fiber tracts.

That there are important nerve centers in the walls of the third ventricle was first emphasized by Edinger, and the recent painstaking studies, particularly by Rioch (1930), have served to locate them in minute detail. From a physiological standpoint, three principal

nuclear accumulations (Beattie) may be distinguished: (1) the supraoptic cluster, (2) the tuberal cluster, and (3) the more posteriorly situated hypothalamic cluster from which pupillary responses, sympathetic in character, can be electrically elicited. Stimulation of the tuberal nuclei, on the other hand, appears to give parasympathetic (vagal) responses; and there is considerable evidence from anatomical as well as physiological studies [54] that the active principle of the neurohypophysis exerts a direct influence on the tuberal as well as on the supraoptic cell clusters.

Though the course of the fibers from these hypothalamic nuclei backward toward the medulla and cord to emerge in the craniosacral autonomic periphery, on the one hand, and in the thoroco-lumbar sympathetic field, on the other, is still obscure, the matter has been attacked in various ways: (1) by tracing the early embryonic development of the finely myelinated fibers coming from these nuclei[1] which are among the first identifiable fibers to be laid down (Cajal, Koelliker and von Gehuchten); (2) by the study of fiber degenerations after experimental lesions (Beattie, Brow and Long); and (3) by stimulatory experiments on serially decerebrated animals (Langworthy and Richter). Though much remains to be learned, the general course of the fibers is now sufficiently clear [*cf.* Spiegel, (37); and Beattie, (38)] to make it apparent that the experimental injuries of Schiff, Ebstein, Keller, and others have served to stimulate or injure the principal descending fiber tracts, but whether the secondary peptic lesions which are under discussion have been due to parasympathetic (vagal) stimulation or to sympathetic paralysis must remain conjectural until more precise information is at hand.

III. PHARMACOLOGICALLY GAINED INFORMATION

a. Clinical interpretations. Through the effect of drugs much of our knowledge of sympathetic and autonomic systems has been acquired. It began with Schmiedeberg's observation, made in Ludwig's laboratory in 1871, that after the injection of nicotine stimulation of the vagus quickened rather than slowed the frog's heart; and subsequently Langley and Dickenson demonstrated (1889–1890) that painting the paravertebral ganglion with nicotine or a nicotine-like substance (pituri) served effectually to block sympathetic impulses passing from the cord. That nicotine has a powerful vagotonic effect can be appreciated by all of those who remember the consequences of their first cigar; and that on the part of habitués excessive smoking among other things is highly disturbing to digestive processes is well known to clinicians and fully recognized if not always admitted by the victims of ulcer themselves.[2]

To Gaskell's pathfinding studies (1886) we owe our present conception of the thoracolumbar sympathetic (the sympathico-adrenal system of Cannon), but it was left for Langley to prove the existence of a separate "cranial outflow" and a "sacral outflow" (his "oro-anal" autonomic or parasympathetic system), the two systems being essentially different in their phylogenetic development and physiological activity [39]. But the conception that there exists in constant operation a physiological antagonism or balance between these two systems appears to have reached its development not in Cambridge but elsewhere. First clearly pointed out by Hans Meyer's pupils, Froehlich and Loewi [40], and subsequently elaborated by Hans Meyer himself [41], this concept became popularized by others who, first and last, have been attached to the Vienna school.

So far as concerns the stomach, the action of adrenalin in checking motility and diminishing secretion is equivalent to a stimulation of the sympathetic apparatus. On the other hand, the action of other drugs, notable among which are pilocarpine and physostigmine, is equivalent to stimulation of the cranial autonomic (parasympathetic) system of which the vagi are the more important branches, and the effects are counteracted by atropin. The several drugs which serve as vagal stimulants are somewhat selective in their action on the

[1] One might well expect that anatomical evidences of the "oro-anal" autonomic (parasympathetic) apparatus would be the first to appear in view of the greater need in the newly born of a buccal and cloacal vegetative mechanism for sucking, digestion, and evacuation, than for an apparatus like the thoroco-lumbar sympathetic, useful in the emergency of escape or combat.

[2] *Cf.* Moynihan, B. Two lectures on gastric and duodenal ulcer, p. 43. Bristol: John Wright & Sons Ltd.

divisions of the parasympathetic apparatus, whereas adrenalin, as Cannon has emphasized, acts explosively on the entire thoracolumbar system at one and the same time.

Since there is no known paralyzant for the sympathetic system (unless ergotoxine may be such) counteractive to adrenalin as atropin counteracts pilocarpine, in studying the effects of lowered sympathetic activity recourse must be had to the experimental extirpation of the prevertebral chain, splanchnic nerves, cœliac plexus, or of the adrenal glands themselves. Sympathetic paralysis thus produced is equivalent in its effects to autonomic (parasympathetic) stimulation due to a release phenomenon; and on the other hand, parasympathetic paralysis theoretically is equivalent to sympathetic stimulation though the effects may be not so evident.

A clinical application of this concept of counterbalance between sympathetic and parasympathetic systems, particularly in relation to the vegetative functions of the pneumogastric, was brilliantly presented [42] by Eppinger and Hess (1910), then colleagues of Hans Meyer in Vienna, in their monograph on "Vagotonia"—a treatise which gave a wholly new interpretation of certain kinds of "nervous invalidism." Vagotonic persons according to their thesis react with sweating and salivation to small doses of pilocarpine; they are apt to be asthenic, to have cardiac arrhythmias, and to show gastric hyperacidity, these symptoms being invariably aggravated by pilocarpine. What is more, the "nervous dyspepsia," gastrosuccorrhœa, pylorospasm, cardiospasm and hunger pains to which vagotonic persons are prone are beneficially affected by atropin. Though Eppinger and Hess briefly discuss the relation of vagotonia to gastric ulcer, they do not expressly state that vagotonia predisposes to ulcer, but on the contrary seem to imply merely that persons afflicted by ulcer in the absence of hyperacidity, hypermotility and so on merely happen to be exempt from constitutional vagotonicity.

The old idea, nevertheless, that a disordered action of the vagus had something to do with ulcer formation had from time to time been revived, and with the increase of knowledge concerning the relation of the nerve to the digestive functions, the belief was held by some that chronic ulcer was the expression of a neurotrophic disturbance—a sort of mal perforans of the stomach. Thus in his discussion of Pavy's theory, that ulcer was due to a chemical imbalance brought about by lowered alkalinity of the blood, Wilks had stated that a neurogenic influence could no more be overlooked than it could in an obviously neurotrophic ulcer of the cornea; and similar ideas have been newly restated in view of the frequency with which ulcer has been observed in tabetics.

But the general ideas formulated by Eppinger and Hess were first definitely focused on spasmodic peptic ulcer in 1913 [43] by Professor von Bergmann who emphasized: (1) that the parasympathetic nervous system is disordered in ulcer; (2) that patients with ulcer respond to pilocarpine more markedly than do normal persons; and (3) that the long continued use of atropin will cure or ameliorate the familiar symptoms which accompany the disease.

This ingenious explanation of ulcer has found favor not only with many clinicians but also with roentgenologists, notable among whom may be mentioned Martin Haudek, of Vienna [44]. In subsequent papers [45] on the subject, von Bergmann, while disclaiming that hypervagotonicity is the cause of *all* ulcers, asserts that they are more common in persons with a neuropathic constitution who show irritability of the secretory and motor functions of the stomach—in other words, in persons with an overactive parasympathetic nervous system. Thus, through a dysharmony or imbalance of the two divisions of the vegetative apparatus the local spasm leading to impaired vascularity of the mucosa that precedes erosions and ulcers is prone to occur.

This novel conception of ulcer pathogenesis, like all other explanations, has found its prompt opponents. Loeper and Marchal [46], for example, in discussing the matter (1926) express the belief that the irritative disturbances on the part of the cranial autonomic system are the consequence rather than the cause of chronic ulcer, which they ascribe to the outpouring of leucocytes (*leucopédèse*) in the submucosa. Simnitzky [47] also (1926),

in calling attention to v. Bergmann's admission that stimulation of the vagus is more active in an acid milieu, and of the sympathetic more active in an alkaline milieu, agrees with Bálint [48] (1926) in ascribing ulcer to primary acidosis of the tissues rather than to dystonia of the vegetative nervous system, which is reminiscent of the early conception held by Pavy and others of ulcer pathogenesis.

1. Substantiation by peripheral action of drugs. Meanwhile, von Bergmann's assistant, Karl Westphal [49], undertook to see if ulcer might not be produced in the lower animals by drugs known to stimulate the parasympathetic system. For this purpose pilocarpine and physostigmine were selected and given subcutaneously to rabbits in toxic doses (cats, dogs, and guinea pigs were less susceptible), localized areas of ischæmic cyanosis being produced leading to erosions from subsequent action of the gastric juice on these vulnerable points. The lesions occurred, however, only when the animal was actively digesting and when the contents of the stomach were acid.[1]

These observations on pharmacologically produced ulcerations, important and suggestive though they are, lie open to the same criticism that applies to other locally produced experimental ulcers in that they emphasize the effects of the drug on the neurosecretory end organs. That vagal stimulants like pilocarpine may appear to act with especial vigor on a parasympathetic center will now be considered.

2. Substantiation by central action of drugs. Following the discovery by Karplus and Kreidl of the Vienna School in 1909 [50] that electrical stimulation of the hypothalamus (doubtless the posterior hypothalamus) caused pupillary dilatation, sweating, and other phenomena indicating a cerebral diencephalic center for the sympathetic nervous system, increasing attention has been paid to the functions of the hitherto much neglected interbrain. In 1925, the interesting observation was made by Cannon and Britton [51] that cerebral decortication in the cat led to an emotional state which they designated "sham rage" from its close resemblance to the behavior of the infuriated normal animal. A prominent feature of these emotional explosions was a mass discharge of the sympathetic nervous system with liberation of adrenalin. Bard [52] subsequently made it clear (1928) that this affective state in decorticated animals depended upon an intact posterior interbrain; and Fulton and Ingraham in turn (1929) showed [53] that a chronic state suggesting "sham rage" was present in cats whose corticofrontal pathways to the interbrain had been surgically divided. Whereas Gaskell had looked upon the thoracolumbar sympathetic as largely a spinal involuntary mechanism, and Langley had carried the cerebral stations of the cranial autonomic apparatus no further headward than the midbrain, these later-day disclosures, indicating that cortically uninhibited affective states emanating from the diencephalon can discharge the sympathico-adrenal apparatus, shed an entirely new light on the subject.

At another time and place [54], certain observations were reported on the effects of injecting posterior pituitary extract (pituitrin) and pilocarpine into the cerebral ventricles. When either the extract or the drug is thus introduced in susceptible (vagotonic?) subjects, it leads to stimulatory effects among which sweating, flushing, lachrymation and excessive, sometimes blood-tinged vomiting were notable features. These effects were interpreted as being essentially parasympathetic in nature and it was assumed, therefore, that the parasympathetic as well as the sympathetic nervous system most probably had a primary nuclear representation in the interbrain.

Whereas pilocarpine supposedly acts exclusively on the nerve terminals, the human tests indicated a far more vigorous, central, and presumably diencephalic action. It accordingly was suggested to my co-worker, Dr. Richard Light, that he try to determine on

[1] Another drug, histamine, which may be regarded as a parasympathetic stimulant in that it causes pronounced flushing with increase of gastric secretion, is more selective in character than pilocarpine; it supposedly acts (Dale *et al.*) on the glands themselves rather than through their nerve supply, and fails to increase gastric motility. Nevertheless Buechner, Siebert, and Malloy, of Aschoff's Institute in Freiburg (Beitr. z. path. Anat., 1928, lxxxi, 391–425) have produced gastric ulcers in starved rats by the injection of histamine. They interpret the observations as favorable to a purely biochemical cause of ulcer—a "correlation disturbance" due wholly to increased gastric acidity. This is a form of hair splitting and the authors in their interesting paper (p. 394) admit that the "correlation disturbance" may be brought about by impulses in the vegetative nervous system.

rabbits whether pilocarpine, introduced intraventricularly, would produce Westphalian erosions in smaller amounts than when given subcutaneously. In collaboration with C. C. Bishop and L. G. Kendall, this matter was put to the test [55], and it was found that even small doses of from 3 to 6 milligrams injected into the rabbits' ventricles produced erosions and that injections of 10 milligrams would cause them in 94 per cent of the animals, whereas 75 milligrams or more were needed to produce corresponding lesions with equal frequency when the drug was given subcutaneously.

The importance of these observations, in my estimation, lies not so much in the fact that a small dose (2 milligrams) of pilocarpine injected into the human ventricles has a prompt and widespread parasympathetic effect, as in the disclosure that pituitrin, when similarly administered, has a corresponding effect. What is more, the response to intraventricular pituitrin, surprisingly enough, is entirely different from the response which follows its intravenous or intramuscular injection. When introduced into the ventricles of susceptible persons, it causes flushing, sweating, salivation, and prolonged vomiting which, like the effect of intraventricular pilocarpine, can be checked by atropin or prevented either by preliminary atropin or by the narcotic drugs (*e.g.* tribromethanol and the barbiturates) which are known to inhibit the hypothalamic centers. When, on the other hand, pituitrin is injected subcutaneously, it causes pallor without sweating and promptly checks gastric peristalsis and secretion, its action in other words being entirely comparable to the effect of adrenalin.[1]

The following roentgenological observations of gastric motility made in collaboration with my colleagues, Dr. M. C. Sosman, and his assistant, Dr. H. F. Hare, have thrown further light on the subject. After a barium meal, the gastric waves as they progress from cardia to pylorus have first been timed, and toxic drugs or extracts have been then administered with results, briefly stated, as follows:

A. Intramuscular injection.

1. Adrenalin (1 c.cm. of a 1:1000 solution) causes an almost immediate cessation of all visible movement for 20 minutes or longer.
2. Pituitrin (1 c.cm. "surgical") has precisely the same effect on the stomach as adrenalin, with cutaneous pallor.
3. Pilocarpine (12 mgm.) also causes a definite diminution of motility associated with moderate sweating.
4. Histamine (1 mgm.) causes a cutaneous flush without sweating and no visible change in gastric motility.

B. Intraventricular injections.

1. Adrenalin (not tried).
2. Pituitrin (1 c.cm. "surgical") promptly accelerates motility and soon causes retrograde peristalsis with retching and vomiting which can be checked by atropin. Other effects are sweating and flushing.
3. Pilocarpine (2 mgm.) causes prompt activation of motility, spasm of pylorus, retrograde peristalsis, prolonged retching, and vomiting. These effects which are associated with a drenching sweat, a cutaneous flush and fall in temperature can be checked by atropin. Vomitus shows increased gastric acidity and positive guiac test for blood.
4. Histamine (2 mgm.: two observations). No visible effect on peristalsis. Sense of fullness in head, dry mouth, no flush, no vomiting.

The assumption that these striking consequences of intraventricular pilocarpine and pituitrin were produced by local stimulation of a center for parasympathetic discharges, has received support from recent observations by Beattie (1932). He has shown [56] on animals that direct electrical stimulation of the region of the tuberal centers in the infundibulum causes not only increased gastric peristalsis and secretion, but, if long continued, leads to small hæmorrhagic ulcers of the mucous membrane near the lesser curvature. After section of the vagi these gastric effects were not obtained.

Thus, the reaction of the stomach to the intraventricular injection of either pilocarpine or pituitrin in man and to direct stimulation of the tuber in animals is hypermotility, hypertonicity, and hyperchlorhydria, these three factors being those that commonly persist in cases of chronic gastric ulcer.

Eppinger and Hess, taking their cue from Langley, did not venture in 1910 to place the

[1] So far as I am aware, there is no other instance of a drug or extract which has contrary effects when administered in different regions of the body: but next to nothing is known of the effects of drugs directly applied to the diencephalic nerve centers. In view of the sensitivity of the vagus nuclei in the fourth ventricle to exceedingly dilute solutions of emetin or apomorphin, it is reasonable to assume that painting the walls of the tuber cinereum with one of these drugs will produce the same or an even more vigorous effect on the stomach.

autonomic control of the vagus higher than the midbrain and felt obliged to postulate the existence of a substance or hormone termed "autonomin" whose continuous activity preserves the normal tonus in the smooth muscles of the vegetative organs—a substance bearing the same relation to the autonomic (parasympathetic) system that adrenalin bears to the thoracolumbar sympathetic. That the secretory hormone of the neurohypophysis (pituitrin), in view of the observations mentioned above, may represent their hypothetical autonomin is not improbable, and the idea at least provides a working basis for further study.

IV. SUMMARY AND CONCLUSIONS

The attempt to find a reasonable explanation for the acute perforative lesions affecting œsophagus, stomach, and duodenum, which in three instances caused early fatality after operations for cerebellar tumor, has led, not only to a review of the extensive literature on the neurogenic aspects of ulcer pathogenesis, but also to certain experimental observations that strongly suggest the presence in the diencephalon of a parasympathetic center. From this center, apparently tuberal in situation, fiber tracts pass backward to relay with the cranial-autonomic stations of midbrain and medulla of which the vagal nucleus is by far the most important because of its influence upon the activity of the lungs, heart, and upper alimentary canal.

Experimental lesions anywhere in the intracranial course of these fiber tracts from anterior hypothalamus to vagal center, presumably from parasympathetic stimulation (or possibly from vagal release due to sympathetic paralysis) are prone to cause gastric erosions, perforations or ulcers (Schiff; Ebstein; and others). Intracranial injuries and diseases affecting these same basilar regions of the brain are known to be accompanied by ulcerative lesions of the upper alimentary canal. It is reasonable to believe, therefore, that the perforations following the cerebellar operations forming the basis of this study were produced in like fashion by an irritative disturbance either of fiber tracts or vagal centers in the brain stem.

Stimulation of the postulated parasympathetic center by intraventricular injections of pilocarpine or pituitrin cause, in man, an increase in gastric motility, hypertonus, and hypersecretion leading to retching and vomiting which ultimately contains occult blood. The same effects, associated with observable patches of hyperæmia of the gastric mucous membrane have been shown (Beattie) to follow direct electrical excitation of the tuber cinereum in animals.

The active principle of the neurohypophysis (pituitrin) demonstrable in the tissues in the form of hyaline bodies, is known to find its way through the infundibular stalk to the region of the nuclear cell masses of the tuber either by direct migration (Edinger; Collin) or by the intermediation of blood sinuses (Popa and Fielding); and the secretory product may possibly pass between the ependymal cells to enter the cavity of the third ventricle (Herring; Cushing and Goetsch; Karplus and Pecznik). What is more, the secretion appears to be under the control of autonomic fibers that pass from the supra-optic nucelus into the posterior lobe. Hence, there is an anatomical basis for the presumption that posterior lobe extract (pituitrin) should have a stimulatory influence on the local vegetative nerve centers. That intraventricular pituitrin would cause a parasympathetic discharge with vagotonic effects, whereas given subcutaneously its action resembles that of adrenalin, could not have been foretold.

The interbrain has been shown (Cannon; Bard) to be the seat of primitive emotions which are normally under cortical control; but in experimentally decorticated animals, probably from release of the sympathetic nucleus in the posterior hypothalamus, there occur explosions of "sham rage" accompanied by a mass-discharge of the sympathico-adrenal system.

The parasympathetic apparatus, in all probability, under normal conditions is likewise strongly affected by cortical or psychic (Pavlov) influences. However this may be, direct stimulation of the tuber or of its descending fiber tracts, or what theoretically amounts to the same thing, a functional release of the

vagus from paralysis of the antagonistic sympathetic fibers, leads to hypersecretion, hyperchlorhydria, hypermotility and hypertonicity especially marked in the pyloric segment. By the spasmodic contractions of the musculature, possibly supplemented by accompanying local spasms of the terminal blood vessels, small areas of ischæmia or hæmorrhagic infarction are produced, leaving the overlying mucosa exposed to the digestive effects of its own hyperacid juices.

Thus it is possible to reconcile the neurogenic theory of ulcerations sponsored by Rokitansky and Virchow's variously modified theory of a primary local cause, whether the lesions are considered in terms of simple erosions, of acute perforations, of autodigestive softening, or of chronic ulcers, and whether they chiefly involve œsophagus, stomach, or duodenum.

Those favorably disposed toward the neurogenic conception of ulcer have in process of time gradually shifted the burden of responsibility from the peripheral vagus to its center in the medulla, to the midbrain, and now to the interbrain, newly recognized as a highly important, long overlooked station for vegetative impulses easily affected by psychic influences. So it may easily be that highly-strung persons, who incline to the form of nervous instability classified as parasympathetic (vagotonic), through emotion or repressed emotion, incidental to continued worry and anxiety and heavy responsibility, combined with other factors such as irregular meals and excessive use of tobacco, are particularly prone to have chronic digestive disturbances with hyperacidity often leading to ulcer—effects wholly comparable to those acutely produced by irritative lesions experimentally made anywhere in the course of the parasympathetic system from tuberal center to its vagal terminals.

While this conception of the etiology of ulcer does not account for all ulcerative processes under all conditions, it offers a reasonable explanation of the majority of them and is in accord with the personal experience of most victims of chronic recurring ulcer. This, briefly, is as near as one can come, with the data at hand, to an interpretation of the neurogenic origin of peptic ulcer and an explanation of its existing prevalence.

BIBLIOGRAPHY

1. Smith, George M. An experimental study of the relation of bile to ulceration of the mucous membrane of the stomach. J. Med. Research, 1914, xxv, 147–183.
2. Jackson, Chevalier. Peptic ulcer of the esophagus. J. Am. M. Ass., 1929, xcii, 369–372.
3. Lindau, A., and Wulff, H. The peptic genesis of gastric and duodenal ulcer, especially in the light of ulcers in Meckel's diverticulum and the postoperative ulcers in the jejunum. Surg., Gynec. & Obst., 1931, liii, 621–634.
4. Beneke, R. Ueber die haemorrhagischen Erosionen des Magens (Stigmata ventriculi). Verhandl. d. deutsch. path. Gesellsch., 1908, 284–294.
5. Wilks, S., and Moxon, W. Lectures on Pathological Anatomy. 3d ed., p. 404. London, 1889.
6. Moeller, S. Die Pathogenese des Ulcus ventriculi mit besonderer Berueecksichtigung der neueren experimentellen Ergebnisse. Ergebn. d. inn. Med. u. Kinderh., 1911, vii, 520–569.
7. Welch, William H. Simple ulcer of the stomach. Pepper's System of Practical Medicine by American Authors, 1885, ii, 512.
8. Hoffmann, C. E. E. Ueber die Erweichung und den Durchbruch der Speiseroehre und des Magens. Arch. f. path. Anat., 1868, xliv, 352–365.
9. Arndt, R. Ein Tumor Cerebri. Arch. f. Psychiat., 1874, iv, 432–464.
10. Idem. Neubildung im Gehirn, Magenerweichung und einfaches oder rundes Magengeschwuer. Deutsche med. Wchnschr., 1888, xiv, 83–85.
11. v. Winiwarter, J. R. Ueber Magen-Darmblutungen nach Operationen. Arch. f. klin. Chir., 1911, xcv, 161–184.
12. Roessle, R. Das runde Geschwuer des Magens und des Zwoelffingerdarmes als "zweite Krankheit." Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1912–1913, xxv, 766–796.
13. Hart, C. Betrachtungen ueber die Entstehung des peptischen Magen- und Zwoelffingerdarmgeschwueres. Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1918–1919, xxxi, 350–380.
14. Mogilnitzky, B. N. Zur Frage der Entstehungsweise und Ursache neurogener Formen des runden Magengeschwuers. Arch. f. path. Anat., 1925, cclvii, 109–118.
15. Korst, L. Das Magendarmgeschwuer und seine Beziehung zu organischen Gehirnerkrankungen. Ztschr. f. d. ges. Neurol. u. Psychiat., 1928, cxvii, 553–561.
16. Elsaesser, C. L. Die Magenerweichung der Saeuglinge. Stuttgart and Tuebingen, 1846, 172 pp.
17. Pott, R. Ueber Tentoriumzerreissungen bei der Geburt. Ztschr. f. Geburtsh. u. Gynaek., 1911, lxix, 674–718.
18. v. Preuschen, F. Verletzungen des Kindes bei der Geburt als Ursache der Melaena neonatorum. (Klinische u. experimentelle.) Festschr. z. Feier d. 50 jaehrigen Jubilaeums d. Gesellsch. f. Geburtsh. u. Gynaek. in Berlin. pp. 359–419. Vienna: Alfred Holder, 1894.
19. Pomorski, J. Experimentelles zur Aetiologie der Melaena neonatorum. Arch. f. Kinderh., 1892, xiv, 165–193.

20. HOLT, L. E. Duodenal ulcers in infancy. Am. J. Dis. Child., 1913, vi, 381–393.
21. GERDINE, L., and HELMHOLZ, H. F. Duodenal ulcer in infancy, an infectious disease. Am. J. Dis. Child., 1915, x, 397–409.
22. DALLA VEDOVA, R. Ricerche sperimentali sulla patogenesi dell' ulcera gastrica. Suppl. al Policlin., 1900, vi, 1153–1156.
23. DURANTE, L. The trophic element in the origin of gastric ulcer. Surg., Gynec. & Obst., 1916, xxii, 399–406.
24. GUNDELFINGER, E. Klinische und experimentelle Untersuchungen ueber den Einfluss der Nervensystems bei der Entstehung des runden Magengeschwuers. Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1918, xxx, 189–229.
25. FINZI, O. Ueber Veraenderungen der Magenschleimhaut bei Tieren nach Nebennierenexstirpation und ueber experimentell erzeugte Magengeschwuere. Arch. f. path. Anat., 1913, ccxiv, 413–432.
26. GIBELLI, C. La funzione delle capsule surrenali in rapporto col processo di riparazione delle fratture e coll' eziologia dell' ulcera gastrica. Pathologica, 1909, i, 131–133.
27. MANN, F. C. A study of the gastric ulcers following removal of the adrenals. J. Exper. Med., 1916, xxiii, 203–210; A further study of the gastric ulcers following adrenalectomy. Ibid., xxiv, 329–332.
28. KEPPICH, J. Kuenstliche Erzeugung von chronischen Magengeschwueren mittels Eingriffen am Magenvagus. Berlin. klin. Wchnschr., 1921, lviii, 414–416.
29. STAHNKE, E. Experimentelle Untersuchungen zur Frage der neurogenen Entstehung des Ulcus ventriculi; zugleich ein Beitrag zur pathologischen Physiologie der Mageninnervation. Arch. f. klin. Chir., 1924, cxxxii, 1–59.
30. KLEIN, E. Left vagus section and partial gastrectomy for duodenal ulcer with hyperacidity. Ann. Surg., 1929, xc, 65–68.
31. SCHIFF, M. De vi motoria baseos encephali inquisitiones experimentales. Bockenheim (Frankfurt a.M.), 1845, 54 pp.
32. Idem. Ueber die Gefaessnerven des Magens und die Function der mittlern Straenge des Rueckenmarkes. Arch. f. physiol. Heilk., 1854, xiii, 30–38.
33. Idem. Leçons sur la Physiologie de la Digestion ii, 416–452. Florence and Turin, 1867. Leçon 35.
34. BROWN-SÉQUARD, C. E. Des altérations qui surviennent dans la muqueuse de l'estomac, consécutivement aux lésions cérébrales. Progrès méd., 1876, iv, 136–137.
35. EBSTEIN, W. Experimentelle Untersuchungen ueber das Zustandekommen von Blutextravasaten in der Magenschleimhaut. Arch. f. exper. Path. u. Pharmakol., 1874, ii, 183–195.
36. BURDENKO, N., and MOGILNITZKI, B. Zur Pathogenese einiger Formen des runden Magen-Darmgeschwuers. Ztschr. f. Neurol. u. Psychiat., 1926, ciii, 42–62.
37. SPIEGEL, E. A. The centers of the vegetative nervous system. Bull. Johns Hopkins Hosp., 1932, l, 237–252.
38. BEATTIE, J. Hypothalamic mechanisms. Canadian M. Ass. J., 1932, xxvi, 400–405.
39. LANGLEY, J. N. The arrangement of the autonomic nervous system. Lancet, 1919, May 13, 951.
40. FROEHLICH, A., and LOEWI, O. Untersuchungen zur Physiologie und Pharmakologie des autonomen Nervensystems. I. Mitteilung ueber die Wirkung der Nitrite und des Atropins. Arch. f. exper. Path. u. Pharmakol., 1908, lix, 34–56.
41. MEYER, H. H. Die Pharmakologie des vegetativen Nervensystems. Med. Klin., 1912, viii, 1773–1777.
42. EPPINGER, H., and HESS, L. Vagotonie; klinische Studie. Samml. klin. Abhandl. ue. Path. u. Therap. d. Stoffwechs.- u. Ernaehr.-Stoerung., Berl., 1910, Hft. 9–10. Also translated in Nervous and Mental Disease Monograph Series, No. 20, 2d ed. New York, 1917.
43. VON BERGMANN, G. Das spasmogene Ulcus pepticum. Muenchen. med. Wchnschr., 1913, lx, 169–174; Berl. klin. Wchnschr., 1913, l, 2374–2379.
44. HAUDEK, M. Ein Beitrag zur Pathogenese und Diagnose der Magen- und Zwoelffingerdarmgeschwuere. Wien. klin. Wchnschr., 1918, xxxi, 202, 286.
45. VON BERGMANN, G. Zur Pathogenese des chronischen Ulcus pepticum. Berl. klin. Wchnschr., 1918, lv, 524–528; Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1923, Suppl. 4, 20–34.
46. LOEPER, M., and MARCHAL, G. Pneumogastrique et ulcère de l'estomac. Presse med., 1926, xxxiv, 17–18.
47. SIMNITZKY, S. S. Neues in der Pathogenese der peptischen Geschwuere. Klin. Wchnschr., 1926, v, 1545–1549.
48. BÁLINT, R. Untersuchungen ueber die Pathogenese des Ulcus ventriculi. Wien. klin. Wchnschr., 1926, xxxix, 7–10.
49. WESTPHAL, K. Untersuchungen zur Frage der nervoesen Entstehung peptischer Ulcera. Deutsche Arch. f. klin. Med., 1914, cxiv, 327–395; *Cf.* also: Underhill, F. P., and Freiheit, J. M. Arch. Path. 1928, v, 411–428.
50. KARPLUS, J. P., and KREIDL, A. Gehirn und Sympathicus. I. Mitteilung. Zwischenhirnbasis und Halssympathicus. Arch. f. d. ges. Physiol., 1909, cxxix, 138–144.
51. CANNON, W. B., and BRITTON, S. W. Conditions of activity in endocrine glands; pseudaffective medulliadrenal secretion. Am. J. Physiol., 1925, lxxii, 283–294.
52. BARD, P. A diencephalic mechanism for the expression of rage with special reference to sympathetic nervous system. Am. J. Physiol., 1928, lxxxiv, 490–515; The central representation of the sympathetic system. Arch. Neurol. & Psychiat., 1929, xxii, 230–246.
53. FULTON, J. F., and INGRAHAM, F. D. Emotional disturbances following experimental lesions of the base of the brain (pre-chiasmal). J. Physiol., 1929, lxvii, Proc. Physiol. Soc., 1929, April 27, xxvii–xxviii.
54. CUSHING, H. The reaction to posterior pituitary extract (pituitrin) when introduced into the cerebral ventricles, etc., etc. Proc. Nat. Acad. Sc., 1931, xvii, 163–180; 239–264.
55. LIGHT, R. U., BISHOP, C. C., and KENDALL, L. G. Production of gastric lesions in rabbits by injection of small amounts of pilocarpine in the cerebrospinal fluid. J. Pharmacol. & Exper. Therap., 1932 [in press].
56. BEATTIE, J. The relation of the tuber cinereum to gastric and cardiac functions. Canadian M. Ass. J., 1932, xxvi, 278.

GEOGRAPHIC PATHOLOGY OF GOITER

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NO modern American treatise on thyroid diseases refers to the variations in form and function of goiter, according to the part of the country in which it occurs. From this fact inferences could be drawn that the morphology and physiology of the North American goiter is rather uniform, although our knowledge about this important subject is very rudimentary.

Systematic comparative studies in Europe have shown that in the different localities of the continent the type of goiter varies widely. In 1921, Klose first aroused interest in the geographic pathology of goiter by calling attention to the peculiarities of the goiter as seen in the midwestern part of Germany. While the Swiss goiter is characterized by large nodes with considerable degeneration and with compression of the surrounding thyroid tissue proper, causing more or less severe symptoms of hypothyroidism or even cretinism, the nodular goiter of the Main valley was described by Klose as consisting of numerous, small, colloid nodules and as being accompanied often by toxic symptoms. In the following year, Aschoff, in whose institute Kloeppel had carried out a comparative study of thyroid glands in the Northern and Southern part of Germany as early as 1909, invited pathologists and clinicians to join in a systematic comparison of normal and goitrous thyroid glands from the different geographical areas. For this purpose the adoption of a uniform nomenclature seemed indispensable and Aschoff recommended a concise, but complete classification. Due to the fact that the leading goiter students of Europe accepted his classification, it was possible to reveal wide variations in form and function of goiters not only in the different regions of Germany, but also in Switzerland, Holland, Scandinavia, and even Russia.

Since Aschoff's classification agrees on the whole with that which has been worked out by American authors, it would be an easy matter to accept it also in this country. It is admitted by many writers that there is, in the recent goiter literature, a bewildering confusion which hinges largely on words rather than on essential facts, but their attempt to remedy it seems to be directed only to the introduction of new terms, thereby increasing the confusion. The general acceptance of an international classification would eliminate confusion, allow a comparison of the various structures of goiter in the different areas of this country, and also facilitate the correlation of the North American goiter with that of other continents. The goiter problem is world wide, but not the same in the different regions, and there cannot be any doubt that the comparative study of the morphology and physiology of goiter not only will be of academic interest, but will open new fields for the practical questions of prophylaxis and treatment.

THE DIFFUSE AND NODULAR FORMS OF GOITER

In Table I, the most common classifications of goiter are brought in correlation with each other. It is evident that Aschoff's nomenclature covers all the different structures found in this country, besides those usually seen only in regions of highest endemicity. Aschoff demands first of all a clear distinction between diffuse and nodular forms of goiter, rejecting the assumption of older writers that the nodular goiter represents a kind of hyperplasia. In his opinion, in nodose goiter one is dealing with a true tumor formation, namely adenomata. According to Aschoff, the nodules of the thyroid gland do not develop from fetal rests, as Woelfler believed, but originate from ordinary thyroid tissue. He admits that the colloid nodule may start out as a localized hyperplastic process and that there is found sometimes a transitional stage between diffuse and nodular goiter, the so called nodular hyperplasia (Fig. 11), but as these nodules increase in size, they assume properties which are typical for new-growths. First they displace more and more the tissue of the sur-

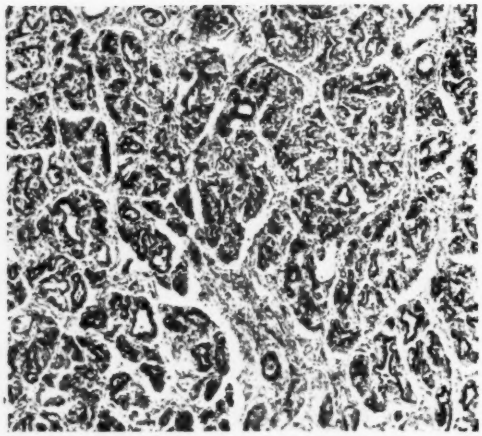

Fig. 1. Congenital diffuse goiter. (South German type.)

Fig. 2. Diffuse parenchymatous (microfollicular) goiter. South Germany, 10 year old boy.

rounding thyroid tissue proper and eventually produce an atrophy by pressure of the neighboring lobules (Fig. 14). By this process they form a more or less distinct capsule which delimits them clearly from the normal thyroid pattern. Furthermore, there is in the nodules from the beginning a complete absence of division in lobules which interferes with nutrition and resorption of the secretion. The lack of a regular drainage system and blood supply accounts for the degenerative processes so commonly found in nodules after they have reached a certain size, and which were erroneously described by the old writers as special varieties: fibrous, hæmorrhagic, cystic, calcified, osseous goiter. It is obvious that the degeneration of the nodules will interfere with the activity of the thyroid gland and from the physiological point of view a clear distinction between diffuse and nodular goiter types appears all the more important.

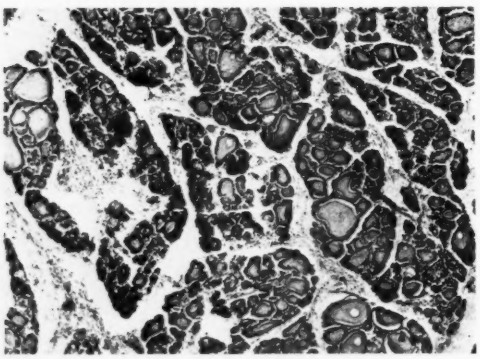

Fig. 3. Diffuse parenchymatous (microfollicular) goiter. South Germany, 19 year old girl.

For the evaluation of the severity of a given goiter endemic, the ratio of diffuse to nodular goiters gives valuable information. It is generally accepted that in a highly goitrous population the nodose goiters outnumber by far the diffuse forms. In de Quervain's clinic, for instance, which draws its material from the center of the Swiss goiter belt, Woelz found 93 per cent nodular goiters, but only 7 per cent diffuse enlargements of the thyroid. In Duesseldorf, which is located in the lower Rhine valley, the frequency of diffuse goiters increases to 32 per cent and on the German sea shore, in Rostock, Hueck found an incidence of 68 per cent diffuse and 32 per cent nodular forms. In Holland there is about an equal distribution of the two different forms, the ratio of diffuse to nodular goiter being 47 to 53 (Josselin de Jong).

Not enough statistics are available in this country, to compare the European figures with the conditions in North America. In Kansas, however, which forms the geographic center of the United States, I found among the

TABLE I.—MOST COMMON CLASSIFICATION OF GOITER

A. Kocher (1919)	Hellwig (1920)	Aschoff (1924)	Wegelin (1926)	McCarrison (1927)	Marine (1927)	Hertzler (1929)	Rienhoff (1929)	MacCarty (1931)
A. Struma diffusa	*A. Hyperplasia of the thyroid*	*A. Diffuse goiter*	*A. Diffuse hyperplasia*					*A. Thyroid shaped*
Struma congenita parenchymatosa	Congenital simple hyperplasia	Congenital diffuse goiter	Struma congenita neonati	Congenital goiter	Simple congenital goiter			
Struma hyperplastica follicularis	Microfollicular Hyperplasia	Diffuse parenchymatous (microfollicular) goiter	Struma diffusa parenchymatosa (microfollicularis)	Parenchymatous goiter	Hyperplasia and hypertrophy			
Struma diffusa colloides	Macrofollicular Hyperplasia	Diffuse colloid (macrofollicular) goiter a. non-proliferant b. proliferant	Struma diffusa macrofollicularis a. resting stage b. proliferant	Diffuse colloid goiter	Involution (colloid goiter)	Uniform stage of colloid goiter	Simple colloid goiter	Hypertrophic colloid goiter
Struma diffusa parenchymatosa papillaris	Exophthalmic goiter	Exophthalmic goiter	Struma diffusa basedowiana	Hyperplastic goiter	Exophthalmic goiter	Exophthalmic goiter	Hypertrophy and hyperplasia of the thyroid	Hypertrophic parenchymatous goiter
B. Struma diffusa et nodosa		*B. Nodular hyperplasia*	*B. Nodular hyperplasia*					
C. Struma nodosa	*Adenomata of thyroid gland*	*C. Nodular goiter*	*C. Adenomata of the thyroid*					*B. Nodular goiter*
Struma nodosa parenchymatosa	Microfollicular Adenoma	Nodular parenchymatous (microfollicular) goiter	Parenchymatous adenomata (trabecular,tubular, microfoll.)	Adenoma	Nodular hyperplastic stage	Mixed tumor (fetal adenoma)	True benign parenchymatous neoplasm of the thyroid	Adenomatous goiter without parenchymatous hypertrophy
Struma nodosa colloides	Macrofollicular Adenoma	Nodular colloid (macrofollicular) goiter a. non-proliferant b. proliferant	Colloid adenomata a. simple macrofollicular b. papillary macrofollicular	Colloid adenoma	Nodular involutionary (colloid) stage	Bosselated stage of colloid goiter	Nodular colloid goiter	
Struma nodosa basedowificata	Adenoma basedowificatum	Nodular goiter with extensive epithelial proliferation	Adenoma basedowificatum		Nodular goiter with hyperplasia	Chronic toxic stage of bosselated colloid goiter (toxic adenoma)	Nodular colloid goiter with hypertrophy and hyperplasia	Adenomatous goiter with parenchymatous hypertrophy

goiters of the Hertzler clinic 53 per cent diffuse and 47 per cent nodular forms. Harms states that of the surgical goiter material in Madison (Wisconsin), 57 per cent are of the diffuse and 43 of the nodular type. Wisconsin and Kansas have, therefore, an almost identical distribution of the two forms of goiter and, as we will see later, the microscopic structure and the physiology of goiter also conform very well in these two geographic areas which are about 600 miles apart.

A somewhat higher percentage of nodular goiter is observed in the surgical material of the Mayo Clinic. Boothby states that in 1924 there were 59 per cent nodular goiters and MacCarty (1931) found nodose forms in 67 per cent of 32,000 goiters. These figures correspond to the low percentage of diffuse goiter in Ann Arbor (Michigan) where Coller encountered only 29.2 per cent diffuse goiters as compared with 70.8 per cent of the nodular form. The incidence of nodular goiter in Michigan is therefore almost as high as at the periphery of the severe Swiss endemic; in Aschoff's institute at Freiburg, near the Swiss border, I found 23 per cent diffuse and 77 per cent nodular goiters. Nowhere however, in North America, does there seem to exist as low a percentage of diffuse goiter as in the mountainous regions of Switzerland (7 per cent), and already from this criterion alone it is obvious that the North American goiter represents an entirely different type of thyroid enlargement, from that seen in Switzerland,

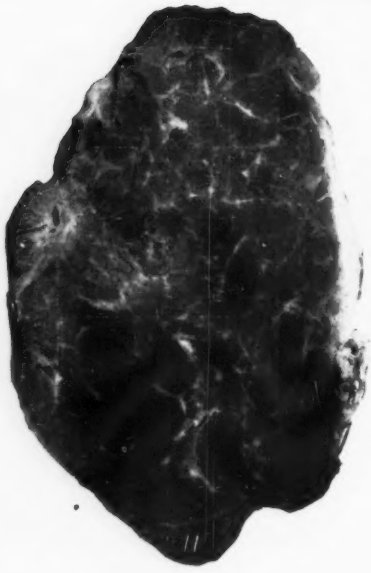

Fig. 4. Diffuse colloid (macrofollicular) goiter.

in the Himalaya mountains, and in other severe endemic areas.

THE PARENCHYMATOUS (MICROFOLLICULAR) AND COLLOID (MACROFOLLICULAR) TYPES OF GOITER

Aschoff divides the diffuse and nodular goiters into the parenchymatous or microfollicular and the colloid or macrofollicular types. The first is characterized by a very small size of the acini, which are lined with cuboid epithelium and their lumina are filled with only scanty amounts of colloid or appear entirely empty. The macrofollicular or colloid goiter type, on the other hand, has large, often irregular acini and the colloid is abundant. In mountainous regions with a high incidence of goiter, the diffuse microfollicular parenchymatous goiters (Figs. 1 and 2) are very common in children and at puberty; they are therefore termed "adolescent goiters" by Gold and Orator. In level regions, however, they are so rare, that most of the American classifications do not even list them. I have never encountered them in my surgical or autopsy material drawn from Kansas, and also Jaffé who examined the thyroid glands of 1,000 autopsy cases at Cook County Hospital, does not mention this type. In areas of high endemicity also, the diffuse parenchymatous goiter (Fig. 3) is rarely seen after the second decade of life and is replaced by the nodular, microfollicular parenchymatous goiter, the so called fetal adenoma (Figs. 17 and 18), which type is really the prototype of mountainous goiter in Switzerland, in the Himalayas, and Pyrenees. In 76 per cent of the surgical material at Bern (Switzerland) parenchymatous nodular goiter was found by Woelz; and Wydler states that 94 of his 104 cretin goiters showed this type of structure. The reverse incidence is seen in level regions with only slight frequency of goiter. In the lower Rhine valley, Orator found only 11.3 per cent of the resected goiters belonging to the microfollicular type, and among the surgical material at Wichita (Kansas), 13.9 per cent of the goiters are parenchymatous. This is still higher than in other areas of the United States. In Wisconsin only 8.3 per cent of the removed goiters were of microfollicular structure and in Ann Arbor still fewer, namely 6.8 per cent (Coller). The parenchymatous, nodular goiter is so rare in North America that Hertzler wants to separate it from the common goiter and proposes

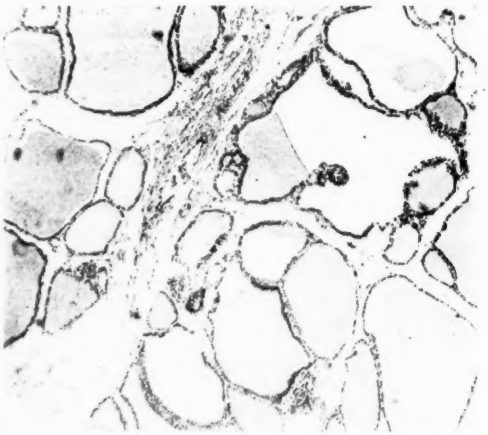

Fig. 5. Non-proliferant diffuse colloid (macrofollicular) goiter.

for it the term "mixed tumor." He regards it as "true neoplasm and not as goiter." This standpoint is limited to the goiter forms as seen usually in level countries and is not justified from a world wide point of view of geographic pathology, because the so called fetal adenoma constitutes actually the most frequent type of endemic goiter seen in regions with high endemicity.

The diffuse and nodular colloid goiter is subdivided by Aschoff into two forms: the non-proliferant (Fig. 5) and the proliferant (Fig. 7). These are not separate entities, but the transitional stages which one observes between them, suggest that both are only different grades of the same functional stage of the thyroid. Also in the non-proliferative form of colloid goiter there are here and there buds of epithelial proliferation in the individual follicles with cubical or almost columnar epithelium and new formation of small daughter acini (Fig. 6). In the proliferant form of colloid goiter these cushion-like proliferations are only more extensive and much more frequent. On account of this epithelial activity, we regard the colloid goiter not as a result of involution and retention of the thyroid secretion, as many still believe, but as a hyperplastic and hypersecretory process. Also the nodular colloid goiter in its earliest stages very often shows epithelial proliferation, a fact which is not in favor of Rienhoff's assumption that the colloid nodules are merely involutionary bodies of a hyperplastic thyroid gland. Figure 15 shows the epithelial wall of the large acini in the colloid nodule in a state of proliferation, the cells being much higher than those of the acini of the surrounding thyroid tissue proper.

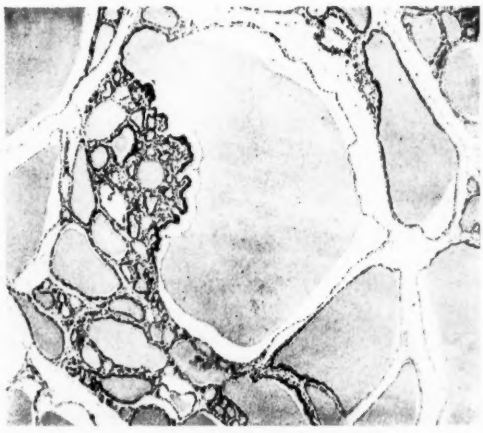

Fig. 6. Non-proliferant diffuse colloid (macrofollicular) goiter. Cushion-like proliferation in acinar wall indicates that the colloid goiter is not the result of retention of colloid only.

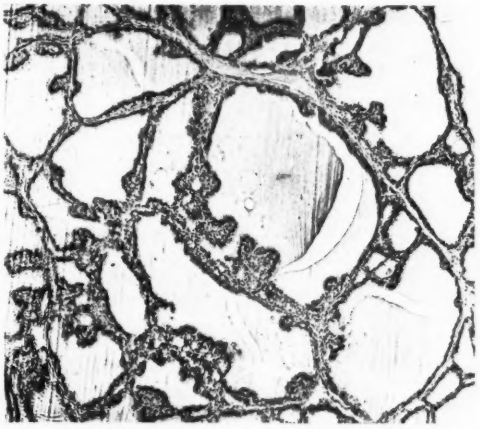

Fig. 7. Proliferant, diffuse colloid (macrofollicular) goiter. Marked epithelial proliferation of the acinar wall.

In level countries, the physiological enlargement of the thyroid gland during puberty and pregnancy—periods of physiologic hyperthyroidism—is anatomically a diffuse macrofollicular colloid type of hyperplasia. After the twenty-fifth year, the diffuse colloid goiter, especially the proliferating form, is very often (in 70 per cent of my own cases) accompanied by symptoms of hyperthyroidism. There is furthermore a close, histological relationship noticeable between the proliferant diffuse colloid goiter and the exophthalmic goiter (Figs. 9 and 10). From the diffuse colloid goiter, transition stages with higher and higher proliferation of the acinar wall lead finally to the classical microscopic picture of exophthalmic goiter. Marine and Lenhart attempted to differentiate primary and secondary exophthalmic goiter, the former originating in a normal, the latter in a goitrous gland. The expediency of this division seems questionable. From my own studies, not only of North American goiters but also of many glands

Fig. 8. Exophthalmic goiter. Dense, gray areas of epithelial hyperplasia in diffuse colloid goiter.

from European patients, I am forced to the belief that exophthalmic goiter develops usually in a diffuse colloid goiter. Many of the exophthalmic goiters I examined, presented on the cut surface, either throughout or in patches, an amber red and translucent appearance suggesting a colloid rich tissue (Fig. 8). In nearly 85 per cent of the glands from patients with Graves' disease, groups of lumina could be distinguished with the unaided eye. These lumina represented large colloid containing follicles such as one never sees in the normal gland, but which are characteristic in the diffuse colloid goiter. Histologically in almost every instance areas with large colloid filled acini were present, either with or without proliferation of the acinar wall. That these changes are not due to an involution caused by Plummer's treatment is indicated by the fact that I saw them also in European material and in exophthalmic goiters obtained from Dr. Hertzler's clinic which were resected prior to the era of pre-operative lugolization.

Clinical and histological studies indicate, therefore, that diffuse colloid goiter—especially the proliferating form—and exophthalmic goiter are two nearly related stages of thyroid activity and that one of them can easily change into the other. Also epidemiologic statistics are in favor of this opinion, since diffuse colloid goiter is commonly associated in the same locality with Graves' disease, while there is little statistical evidence in regard to the association of thyreotoxicosis with diffuse or nodular microfollicular parenchymatous goiter.

The nodular colloid goiter also is often the cause of toxic symptoms, especially if the nodules are very small, without distinct fibrous capsule and without higher grades of degeneration, such as seems to be the rule with the North American type. While it is usually not difficult in a given case of diffuse goiter to

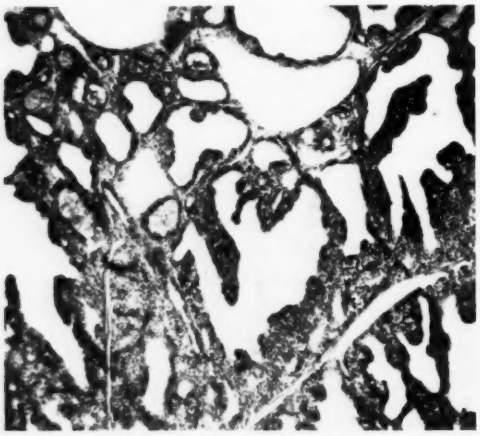

Fig. 9. Exophthalmic goiter. Acini appear empty. Specimen obtained before era of Plummer's pre-operative treatment with Lugol's solution.

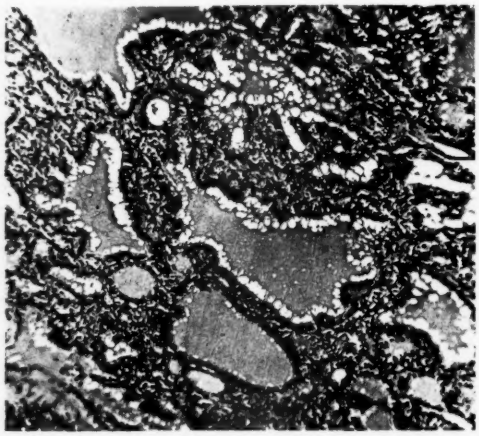

Fig. 10. Exophthalmic goiter, resected after administration of Lugol's solution. The acini are filled with dense colloid. The hyperplasia is still marked.

Fig. 11. Nodular hyperplasia. Transitional stage between diffuse and nodular goiter.

correlate the microscopic picture with the clinical symptoms, we must use great care in drawing conclusions concerning the function of a nodular gland. It seems almost impossible in a specimen with many—sometimes more than a hundred nodules of different structure—to get a correct impression of the histological character of the whole gland by examining sections from only a few different areas. But there is general agreement that the nodular colloid goiter of the level countries also is often accompanied by hyperthyroidism. Among the goiter patients of the Hertzler clinic, 60 per cent of those with non-proliferant, and 85 with

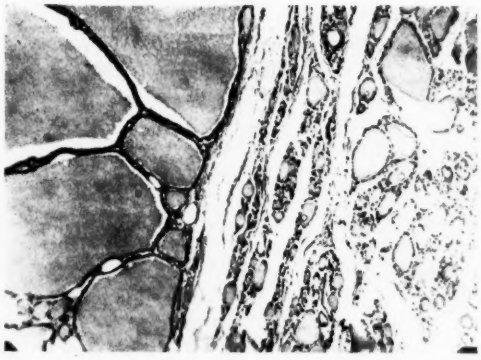

Fig. 13. Non-proliferant, nodular colloid (macrofollicular) goiter. The epithelium in the nodule is higher than in the thyroid tissue proper. The latter is compressed.

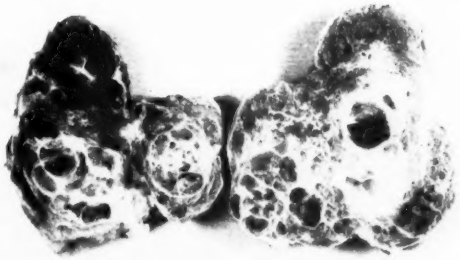

Fig. 12. Nodular colloid (macrofollicular) goiter. Small size of nodules, very thin capsule, absence of higher grade of degeneration are characteristic of the North American goiter.

proliferant nodular colloid goiter showed definite toxic symptoms. Table III illustrates the high incidence of diffuse and nodular colloid goiters as compared with the microfollicular structures in level countries, and in Table IV the frequency of thyreotoxicosis is listed according to the different localities.

We learn from these tables that in mountainous regions the nearer one approaches the center of the goiter endemic, the less he meets the colloid goiter. We find there as a prototype of goiter during childhood the diffuse parenchymatous (microfollicular) goiter, while in adults the parenchymatous nodules prevail. Thyreotoxic goiter is an exception in these regions, and we understand that Wegelin, who

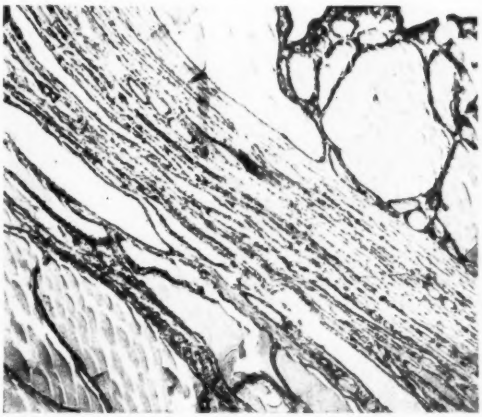

Fig. 14. Capsule formation between two colloid nodules. This formation consists of compressed thyroid tissue proper.

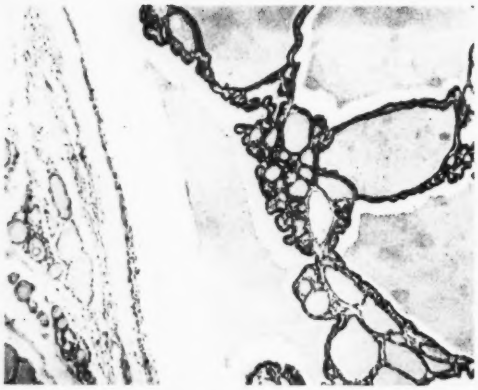

Fig. 15. Proliferant, nodular colloid (macrofollicular) goiter. Marked epithelial proliferation in the nodule. No evidence of "involution" (Rienhoff).

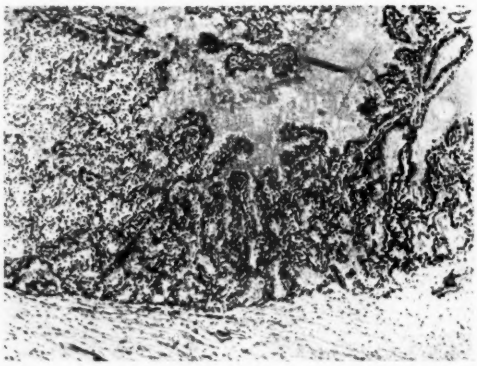

Fig. 16. Nodular colloid goiter with marked epithelial proliferation. "Adenoma basedowificatum" of the European literature.

lives in the center of the Swiss goiter endemic, regards exophthalmic goiter as a special entity of thyroid disease which has no relation to the common endemic goiter. This view, however, will not hold, if one considers the peculiarities of the goiter typical for level countries. Here, as in North America, exophthalmic goiter and toxic nodular goiter are very common and they develop apparently on the basis of the most frequent type in these level regions, the macrofollicular colloid goiter. The underlying cause of Graves' disease and toxic goiter is not a constitutional thymico-lymphatic anomaly, as Warthin and Simpson hypothecate, but the diffuse, nodular colloid goiter itself is the essential organic factor predisposing to thyreotoxicosis.

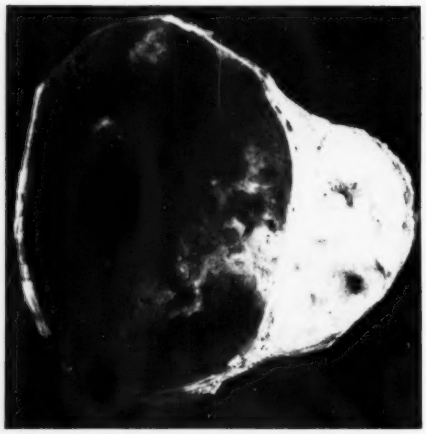

Fig. 17. Nodular parenchymatous (microfollicular) goiter. "Fetal adenoma" of the older writers. It is very common in regions with high endemicity, very rare in level countries.

COMMENT

A systematic comparative study of the North American goiter has not yet been under-

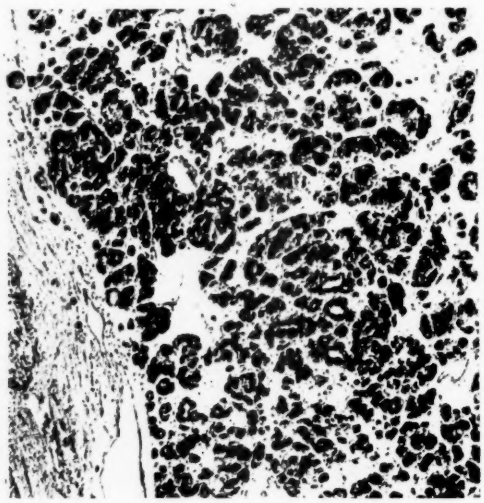

Fig. 18. Nodular parenchymatous (microfollicular) goiter. The acini in this type are almost solid, sometimes tubular. Hyaline degeneration of the center.

TABLE II.—INCIDENCE OF DIFFUSE AND NODULAR GOITER

Locality	Author	Diffuse Goiter	Nodular Goiter
Bern (Switzerland)	Woelz	7	93
Duesseldorf (Lower Rhine Valley)	Orator	35	65
Rostock (North German Sea Shore)	Hueck	68	32
Utrecht (Holland)	de Jong	47	53
Halstead (Kansas)	Hellwig	53	47
Madison (Wisconsin)	Harms	57	43
Rochester (Minnesota)	Boothby MacCarty	41 32.2	59 67.8
Ann Arbor (Michigan)	Coller	29.2	70.8

TABLE III.—RELATIVE FREQUENCY OF COLLOID, EXOPHTHALMIC AND PARENCHYMATOUS GOITER

Locality		Colloid Goiter	Exophthalmic Goiter	Parenchymatous G.
Bern	Woelz	26.3	3	70.7
	Wydler	8.5	.....	91.5
Duesseldorf		73.6	15.1	11.3
Halstead (Kansas)		68.4	16.7	13.9
Madison (Wisconsin)		76	14.7	8.3
Ann Arbor (Michigan)		78.6	10	6.8

TABLE IV.—INCIDENCE OF GOITER WITH THYREOTOXICOSIS IN DIFFERENT REGIONS

Locality	Author	Frequency of Thyreotoxicosis Per cent
Bern (Switzerland)	Woelz	3
Duesseldorf	Orator	44
Danzig (Baltic Sea shore)	Liek	50
Stockholm (Sweden)	Troell	57.3
Halstead (Kansas)	Hellwig	65.6
Madison (Wisconsin)	Harms	71.3
Dayton (Ohio)	Simpson	56.1
Ann Arbor (Michigan)	Warthin	42.1
Rochester (Minnesota)	Plummer (1913) Boothby (1924)	68 51.3
Portland (Oregon)	Menne	67.5

taken and the statistical data which are available on the variations of form and function of goiter according to different geographic areas are very meager. From the few facts which are known, it would appear that the North American goiter does not vary in different regions as widely as does the European. There are three outstanding characteristics which distinguish the North American goiter from the types seen in mountainous regions with high endemicity: (1) A relative frequency of diffuse enlargement of the thyroid gland; (2) the absence of congenital microfollicular goiter and the scarcity of microfollicular nodules, the so called fetal adenomas; (3) the high incidence of macrofollicular colloid goiters. The last characteristic is, I believe, closely related to a very marked frequency of Graves' disease and nodular toxic goiter in this country.

In this paper, only data from surgical material were used and they cannot be regarded as conclusive before they are completed by autopsy findings, since only anatomical studies in the postmortem room will embrace all age groups and thereby variable factors, pertinent to surgical material, will be excluded (Jaffé, Orator).

A thorough knowledge of the variations in structure and function of goiter according to the locality will necessarily influence also our conception of the etiology of this world wide disease and will be of benefit in solving practical problems, prophylaxis, and treatment.

The present tendency of goiter students to use their own nomenclature and to introduce new terms with every new publication should be discouraged, since it does not permit a systematic comparison of the various structures of goiter in different geographic areas. For a successful comparative study of goiter the use of a uniform nomenclature seems imperative and Aschoff's classification which, in 1927, at the International Goiter Conference in Bern found the unanimous consent of all leading goiter students, should be generally accepted also in this country.

CONCLUSIONS

1. The morphology and physiology of the European goiter varies widely according to the different regions.

2. The few statistical data available for North America seem to indicate that the goiter type in this country is rather uniform, but very different from that in regions of high endemicity (Switzerland, Himalayas, Pyrenees).

3. In Kansas and Wisconsin, there are more diffuse than nodular goiters among surgical patients.

4. Congenital parenchymatous goiter is absent. The diffuse enlargement of the thyroid during puberty and pregnancy represents a diffuse colloid goiter.

5. Parenchymatous nodules of the thyroid gland—the fetal adenomas of the older writers—constitute only 6 to 14 per cent of resected goiters.

6. The most common structure of goiter in North American surgical material is the diffuse and nodular colloid goiter (68 to 79 per cent).

7. Thyreotoxic symptoms, accompanying goiter, are more frequent in this country than in any other so far studied (70 per cent of the surgical cases).

8. The North American goiter resembles the goiter forms as found in European level countries (Northern part of Germany, Holland, Russian lowland).

9. A systematic comparison of the morphology and physiology of goiter in many different areas of North America seems to be of great practical importance and for its success the acceptance of a uniform classification appears essential.

BIBLIOGRAPHY

1. Arndt. Der Kropf in Russland. Jena: G. Fischer, 1931.
2. Aschoff. The Goiter Problem. Lectures on Pathology. New York: P. B. Hoeber, 1924.
3. Boothby and Sandiford. Basal metabolism. Physiol. Rev., 1924, iv, 69.
4. Coller. The morbidity of endemic goiter. J. Am. M. Ass., 1924, lxxxii, 1745.
5. Harms. Grundumsatz und histologischer Befund bei 200 nordamerikanischen Strumen. Arch. f. klin. Chir., 1930, clix, 317.
6. Hellwig. Die diffuse Kolloidstruma. Mitt. a.d. Grenzgeb., 1920, xxxii, 508; Form und Funktion des nordamerikanischen Kropfes. Arch. f. klin. Chir., 1929, cliv, 1.
7. Hertzler. Mixed tumors of the thyroid gland (fetal adenomas). Arch. Surg., 1928, xvi, 1187.
8. Huber, H. Comptes Rendus de la Conférence internationale du Goitre. Bern, 1928.
9. Hueck, H. Zur Frage des Parallelismus zwischen klinischem und histologischem Bild der Struma. Arch. f. klin. Chir., 1924, cxxx.
10. Jaffé. The variation in weight of the thyroid gland and the frequency of its abnormal enlargement in the region of Chicago. Arch. Path., 1930, x, 887.
11. Josselin de Jong, R. Ueber Kropf in den Niederlanden. Beitr. z. path. Anat. u. z. allg. Path., 1925, lxxii.
12. Kloeppel. Vergleichende Untersuchungen ueber Gebirgsland-und Tieflandschilddruese. Beitr. z. path. Anat. u. z. allg. Path., 1910.
13. Klose. Ueber Ursachen, Typen und Behandlung des Kropfes. (Ein Beitrag zur geographischen Chirurgie des Maingaukropfes). Med. Klin., 1921, No. 26.
14. Kocher, A. Kropf; in Kraus und Brugsch, Spezielle Pathologie und Therapie innerer Krankheiten. Vol. i. Berlin and Wien, 1919.
15. MacCarty. Pathologic classification of goiter and its clinical significance. Ann. Int. Med., 1931, v, 178.
16. Orator und Schleussing. Schilddruese und Kropf am Neiderrhein. Jena: G. Fischer, 1931.
17. Wegelin. Schilddruese; in Henke-Lubarsch's Handbuch der spezielle Pathologie, Anatomie und Histologie. 1926, viii.
18. Woelz. Vergleichende Untersuchungen ueber die Haeufigkeit der verschiedenen Kropfformen in Basel und Bern. Schweiz. med. Wchnschr., 1921, No. 27.
19. Wydler. Die Histologie der Kretinenstruma. Jena: G. Fischer, 1926.

A NEW METHOD FOR GRAPHICALLY RECORDING THE CONTRACTIONS OF THE PARTURIENT HUMAN UTERUS

A Study of the Effect of Certain Sedatives, Anæsthetics, and Stimulants Upon the Uterus in Labor[1]

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J. MATTHEWS DUNCAN, lecturer in midwifery in Surgeons' Hall Medical School, Edinburgh, during the middle of the last century was the first it seems of whom there is any record as having attempted to demonstrate experimentally the uterine force exerted in labor. His work consisted essentially in ascertaining the amount of force necessary to rupture fresh fetal membranes by measured water pressure, which he regarded as a fair index to normal or "natural labor." For the extreme pressures he recorded, by a dynamometer, the amount of force necessary to be exerted in forceps extraction, during the uterine contractions. His figures arranged in excellent tabular form fall well within the large range of since variously estimated pressures as from 4 to 400 pounds (Williams). He did not measure the uterine forces directly. Among his writings, however, one discovers that he did realize the possibility of direct measurements and although he seemed somewhat reluctant to try the method which he suggested, he did describe it.

Two years before Duncan's excellent book appeared, Carcassone is said to have presented an instrument for measuring the uterine contractions before the French National Academy of Medicine. He called his instrument the *metrodynamometre* but no description of it seems to have appeared, nor are there any records of the work done with it.

It remained for Friedrich Schatz, of Germany, in 1872, to perfect a method for obtaining permanent graphic records, by internal hysterography, of the force and nature of the uterine contractions in labor. His work is classic and no investigation or literature pertaining to the physiology or dynamics of the parturient human uterus is complete without full regard for his methods, his results, and his deductions. He used a small rubber bulb or *Kolpeurynterblase* of from 70 to 80 cubic centimeter capacity which was filled with water and was connected in a closed measured system, by means of a T-tube to a revolving recording drum, and to a calibrated mercury manometer. Preferably under chloroform anæsthesia, the bulb was introduced into the uterus, past the presenting part, to the abdominal surface of the fetus, care being rigidly exercised not to rupture the membranes. By this method he was able to get, simultaneously, the force in millimeters of mercury exerted by the contracting uterus upon the rubber ball, as well as a permanent, timed tracing of the contractions and relaxations. His tracings demonstrate the pressures exerted in the several stages of labor; the duration of the increment, acme, and decrement of the contractions; and the influence of the addition of abdominal pressure.

Eight years after Schatz, Poullet, of France, constructed an apparatus which he called the *Tocograph*, with the help of which he hoped to determine not only the forces exerted by the uterus in labor, but also the additional forces contributed by the abdominal muscles. To this end he introduced a rubber bulb or balloon into the uterus and one into the rectum, above the presenting part, each of which was connected by tubing to a recording quicksilver manometer. Floats and writing points were adjusted to the surface of each column of mercury, and tracings were made upon Ludwig's kymograph. It does not appear that his results, by these studies, were sufficiently successful to permit convincing conclusions.

Polaillon, a contemporary of Poullet, used a small india rubber balloon, but unlike Schatz, he placed it just within the cervix and used a Marey tambour for recording. His work seems to have been more reliable than that of Poullet. In order to account for acces-

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Fig. 1. A composite picture showing the uterus before and during a contraction. (De Lee. Courtesy W. B. Saunders.)

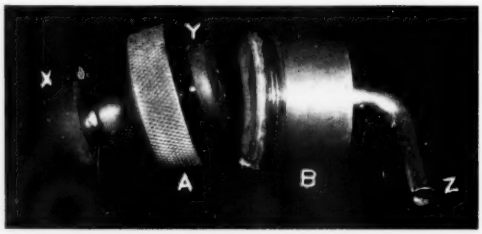

Fig. 2. Pneumatic chamber, *B*, unscrewed from plunger sheath, *A*, to demonstrate plunger, *XY*, and rubber diaphragm. The outlet tube, *Z*, is connected to the writing system by rubber tubing. ×1.28.

sory uterine movements, he divided them into extrinsic and intrinsic, the latter being the irregular fetal movements; and the former made up of such extra-uterine activities as coughing, sneezing, deep sobbing, transmitted maternal arterial pulsations, bearing down efforts, and movements of parts of the maternal skeleton as might cause additional abdominal pressure.

In 1891, Acconci, an Italian, using an apparatus similar to Polaillon's, made several determinations of the action of various agents on uterine contractions, and Doehnoff, a German, in 1892 demonstrated, also graphically, that chloroform had a definite depressant action upon contractions of the uterus in labor, in direct proportion to the depth to which that anæsthetic was administered.

F. Westermark (1893) seems to have been the first investigator who objected to the methods used by some of his predecessors and contemporaries in the field of study under review. He argued that to introduce a rubber bulb or balloon of a large capacity (70 to 80 cubic centimeters) into the uterus, gave rise to the dangers of intra-uterine manipulations; that it caused increased uterine contractions above the normal due to the bulk added to the contents of the uterus, and that it was necessary to anæsthetize each patient in order successfully and satisfactorily to introduce the bulb into its proper position in relation to the fetus and membranes.

To overcome these pertinent objections, Westermark used a small rubber bulb similar to the nipple of a child's nursing bottle, of a capacity of 2 cubic centimeters, which he attached to a urethral catheter. Using this apparatus and a drum recording mechanism, he made many very satisfactory and exhaustive observations upon the duration of labor, the various phases of labor, and labor pains, as well as the height to which the uterine forces rose, in millimeters of mercury, during the acme of each pain.

A departure from all of the procedures mentioned to record uterine contractions was first taken by Ruebsamen, of the Frauen Klinik, Dresden, in 1913, during his studies of the action of pituitary extracts especially in the third stage of labor, but no description of his method was published until 7 years later. In 1920, he included, in a report concerning the clinical and experimental action of quinine, hydrastis, and crotarnin, a method called "external hysterography," which demonstrates an anxious desire to get away from unnecessary experimental intra-uterine manipulations. The method is no doubt of value for studies conducted postpartum, but its many shortcomings for use in observations conducted during the first and second stages of labor are at once apparent.

The apparatus is essentially a device of known weight which is carefully adjusted and supported on a frame by a cord and pulley so that it rests on the abdomen, covering the uterus. Apparently, when the uterus contracts, the weight is lifted, and by means of the cord the evenly balanced writing arm of a timed revolving recording drum, to which it is attached, is raised and a tracing is made.

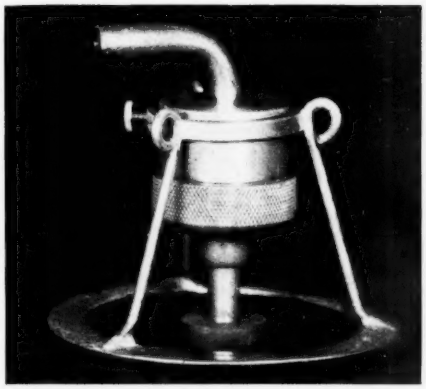

Fig. 3. Air chamber and plunger in tripod support.

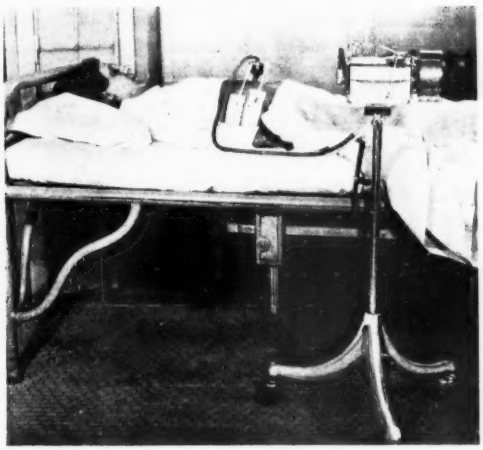

Fig. 4. The hysterograph applied to the abdomen of a patient in labor. The recording apparatus is also set up.

It goes without further comment, that it is indispensable for the patient to lie absolutely quietly, since moving from side to side will alter the support given to the weight; that coughing, vomiting, or sneezing may also displace the weight; and that the bed upon which the patient lies may not be moved. It may, of course, be assumed that these ideal circumstances may be found among extremely co-operative patients during and after the third stage of labor, but it is almost impossible to conceive that one could ever get a sufficient number of patients during the first and second stages of labor who would be ideal subjects, to allow that the apparatus has any value as a routine method to record the contractions of parturition.

Aleck Bourne and J. H. Burn are the most recent contributors to the graphic study of the action of the parturient human uterus. Most of their work deals with the action and dosage of pituitary extract and the ergot alkaloids on the uterus in labor. Their efforts, in 1927, toward the standardization of the unit dose of pituitary extracts were a decided contribution to the best obstetrical literature. In July, 1930, their most recent article appeared in which they used their original method of a water filled system consisting essentially of a rubber intra-uterine bag and stem, and a drum recording apparatus to determine the action upon the human uterus, of several commonly used drugs and anæsthetics.

In the United States, M. Pierce Rucker, of Richmond, has perhaps contributed more than anyone else to the graphic study of the human uterus in labor. His most inclusive reports embrace the influence of various anæsthetics and analgesics on the contractions of the uterus; the action of pituitary extract and thymophysin; and the effect of ergot. He took the opportunity, whenever he had occasion to insert the hydrostatic bag (Voorhees bag) into the cervix of one of his patients, to connect the stem of the bag with a mercury manometer by means of a thick wall rubber tube. The free arm of the manometer was fitted with a float that carried a writing point and inscribed its movements on a revolving smoked drum.

A NEW METHOD FOR EXTERNAL HYSTEROGRAPHY

When the investigation with which this paper is concerned was first considered, it was believed that if any satisfactory method could be found whereby tracings of the uterine contractions might be recorded without subjecting patients to unnecessary intra-uterine manipulations, it would be easily possible to collect sufficient data in a relatively short time with very little if any hardship to subjects or inconvenience to nursing assistants. It was realized, especially, that every patient,

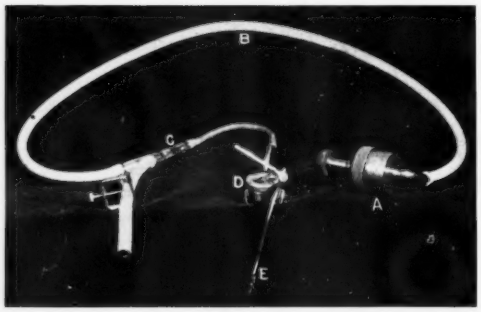

Fig. 5. The pneumatic chamber and plunger, *A*, are connected by rubber tubing to the sensitive tambour, *D*, upon which is mounted the writing arm and ink point, *E*. The glass Y-tube, *C*, allows for a free arm which may be released during adjustments.

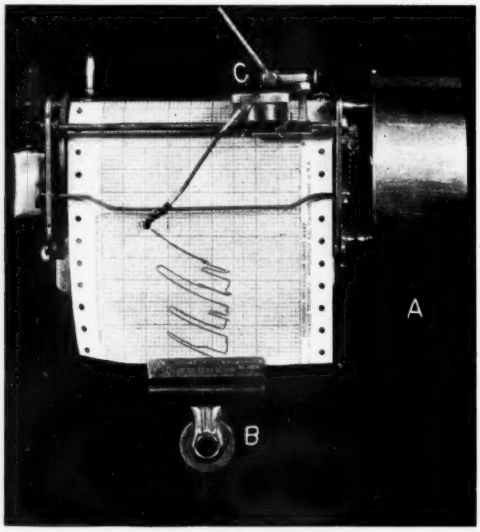

Fig. 6. The writing arm and ink point mounted on the recording apparatus with the tambour, *C*. The ruled paper controlled by the clock, *A*, and weight, *B*, mechanism moves at the rate of 1 inch every 5 minutes, each small square being equivalent to one half minute.

were she to have a hydrostatic bag inserted for purposes of study, would consequently be subjected to at least one additional period of anæsthesia; and that she would be jeopardized by the hazards of vaginal examination and cervical manipulations, relatively insignificant as they may be in a well conducted maternity surgery. This last method of study if it were to be done on a large enough scale to be of any value, would require the frequent services of assistants to prepare the patient, sterilize and prepare the colpeurynter set-up, anæsthetize the patient, and assist with the attachment of the recording apparatus to the stem of the bag. Valuable opportunities might be lost too, to study a certain patient at a certain time, if at that time delivery activities were so great—as very frequently occurs—as not to be able to have available a delivery room team.

From the viewpoint of study, it was felt that the presence of a hydrostatic bag in the uterus or cervix, causing, as it nearly always does, added stimulation to the force and frequency of labor contractions, would not give a fair estimation of the uninfluenced uterus; and that it would be impossible to study the normal effect of drugs which are said to stimulate the induction of labor and the intensity of established contractions.

It was realized too, that an apparatus to be successfully used in routine external hysterography must be so constructed as to be insensitive to normal breathing, pulsations transmitted from the abdominal aorta, and ordinary movements of the patient. It should also be light in weight, not cumbersome or annoying to the subject, and easily placed and fixed in position on the abdomen during any stage of labor without interfering with, or retarding, the course of progress.

Such an apparatus was constructed first of brass and then of aluminum from suggestions made by Professor Sollmann, and with the assistance of Mr. Morris Dann, of the Department of Pharmacology of the Western Reserve University Medical School. I have used it exclusively with complete success and satisfaction for the accumulation of all the data presented in this report. The principle upon which it is based is that during each uterine contraction the anteroposterior diameters of the uterus and the maternal abdomen are increased—the more severe the contraction the greater the increase (see Fig. 1). Advantage has been taken of these phenomena by fixing the plunger and diaphragm of a closed air system to the abdomen, so that each contraction causes a compression of the

Fig. 7*. Normal first stage tracings in primipara showing double contractions and fetal move ments; left occipitoposterior position, three fingers' dilatation. *A*, No analgesia or anæsthesia; *B*, contractions painful, patient comfortable between pains; *C*, patient more uncomfortable between pains and complaining during contraction; *D*, patient very uncomfortable and complaining.

*The tracings shown in Figures 7 to 25 have been redrawn to produce better printing plates. Photographs of the original tracings appeared in the thesis.

air which in turn affects a sensitive rubber tambour supporting a writing point.

Figure 2 illustrates the plunger section of the apparatus and the air-chamber, which have been unscrewed from one another to allow one to see the way in which the rubber dam is attached and to make more vivid the relationship which the internal end of the plunger bears to the diaphragm when inward pressure is made against the external end. The metal outlet tube, *z*, allows the air, compressed in the chamber, to be transmitted to the recording system. These parts of the apparatus are screwed tightly together, and supported on the abdomen in a tripod-like structure, which is fixed by tapes tied in the eyelets of the tripod and held fast by adhesive straps to the patient's loins (Figs. 3 and 4).

The apparatus is applied to the abdomen over the point of maximum contraction and bulging which most frequently is in the immediate neighborhood of the umbilicus, and by increasing or decreasing the tension on the tapes, as well as by lowering or raising the apparatus in the support by means of the set screw the plunger is set approximately half its length within its sheath. The metal outlet tube is then connected by rubber tubing to the writing tambour (Fig. 5). A glass Y-tube is placed in this circuit so that the free arm may be opened during the manipulations of adjustment, thus relieving any adventitious compression of the air, from handling or squeezing the tubes, before the study is begun. Before each study, the entire air system is immersed in water to detect air leaks which are repaired at once.

Abdominal respiratory movements and fluctuations of the abdominal wall due to pulsations transmitted from the maternal aorta, do not affect the plunger. The entire apparatus with its tripod support rests on the evenly undulating movements of the abdomen in the intervals between contractions similar to the way in which a moored skiff rests upon the ripples of a calm lake. Violent contractions of the abdominal muscles, voluntary or involuntary, or increase in the intra-abdominal pressure due to hard coughing, vomiting, or bearing down efforts cause additional compression of the column of air in the system and superimposed lines on the corresponding tracings. Fetal small parts, when they move directly under or very nearly adjacent to the plunger, also cause a very transitory variation in the tracings.

The sensitive tambour, upon which is supported a writing arm with a small glass pen, is part of the recording apparatus (Fig. 6) modified by Mr. Dann from a similar apparatus manufactured by the Toledo Technical Appliance Company, Toledo, Ohio, which was designed by him, and Doctor Harry R.

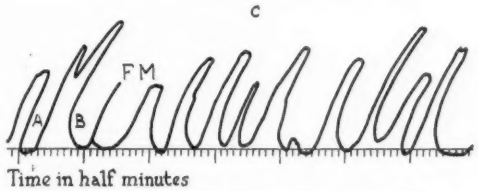

Fig. 8. Normal first stage contractions of a primipara, no anæsthesia, no analgesia. Points *A* and *B* indicate where pain was felt and where it disappeared, respectively. Note the irregular intensities, double contractions, and fetal movements, *FM*. *C*, Cervix dilated 3 fingers.

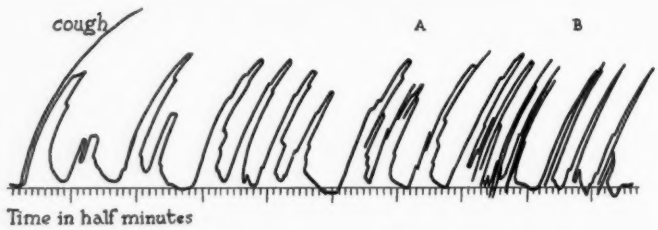

Fig. 9. Transition from first to second stage. Note the superimposed tracings caused by increased pressure or "bearing down" at *B*. Patient was a primipara; vertex presentation; no anæsthesia or analgesia.

Trattner of the Department of Genito-urinary Surgery, Cleveland City Hospital, to record the contractions of the human ureters and the rate of urine flow. The ink point inscribes its tracings upon a continuous roll of white metabolator paper which is ruled in tenths of inches. The unrolling of the paper is accomplished by a revolving cylinder at the ends of which are evenly spaced, spiked cogs which fit into the holes on the edges of the paper. The cylinder is made to rotate by means of a clock and weight mechanism so that one inch of the paper passes a given point in 5 minutes, each tenth of an inch ruling, therefore, representing one half of each minute.

It is possible with this specially ruled paper easily and readily to read off the time factors in any particular study, such as the intervals between contractions, the duration of time from beginning to end of each contraction, the time necessary for any particular drug or agent to affect the tracings, and so forth.

No concern has been given to measuring uterine forces by the mercurial manometer.

None of the patients complained of any great discomfort due to the weight or presence of the apparatus, and they often manifested considerable interest in watching the "pictures of their pains," or learned to prepare themselves for a pain when they saw the writing point begin to rise from the base line of relaxation during the short interval before a contraction was sufficiently intense to arouse central registration of pain.

Nearly fifty individual studies were completed at the time of this writing. Tracings were made in the first and second stages of labor under varying circumstances, and the clearest specimens of each class photographed for reproduction in this report.

CHARACTERISTIC TRACINGS

The Uninfluenced or Control Uterus in Labor

The human uterus, just as all other non-striated muscular organs, is independent of the will of the patient, and its contractions can not, therefore, be diminished or increased by her volition. The uterus contracts painlessly throughout the greatest span of life of the human female and even in intra-uterine life—

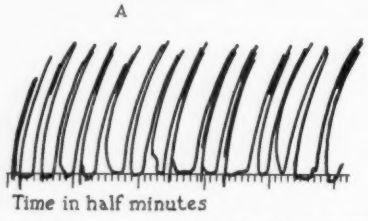

Fig. 10. Typical second stage tracing when no analgesia or anæsthesia has been given. Patient was a primipara and the cervix was fully dilated. *A*, Voluntary bearing down.

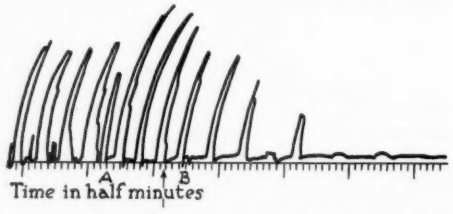

Fig. 11. Effect of ether on the uterine contractions of a multipara, vertex presentation, in labor. Point *A* indicates the beginning of the second stage of labor and the arrow indicates the commencement of drop ether.

Fig. 12. Ether as an analgesic has no effect upon the progress of labor when given during contractions. *A*, Inhalation of approximately 1 dram of ether during each pain; *B*, patient is more comfortable during pains; *C*, membranes intact, nearly fully dilated cervix; *D*, vomiting; *E*, patient comfortable during pains, ether continued; *F*, cervix fully dilated, delivered shortly thereafter.

except in pathological changes of its contour or cells, and in labor. Ko Chi Sun, in his work on the spontaneous contractions of the human uterus, at Johns Hopkins University, was able to demonstrate these facts beautifully in subjects ranging from a 6 months fetus to women of the climacteric.

The painless intermittent contractions which also persist all through pregnancy become painful and increase in intensity of force and frequency of recurrence during the progress of labor. The contractions, as a rule, are at the onset not very fierce and recur at intervals of from 15 to 20 minutes. As labor progresses, the contractions grow stronger and more frequent, and whereas at first the patient may have experienced some discomfort and feeling of fullness in her lower back, she now begins to complain of pain and may beg for relief.

When labor is well established the uterus contracts at intervals of from 1½ minutes to 4 minutes. Each contraction reaches its maximum slowly, but the acme is maintained only a relatively short period of time before relaxation sets in. The whole time which transpires from the beginning of a contraction to the point of complete relaxation varies in different patients and at different times during a single labor. Contractions also may be double; that is, somewhere before a contraction has reached a point of complete relaxation the uterus may contract again, the second contraction sometimes being more painful and intense than the original. Contractions, too, are not all of the same degree of intensity, especially in the first stage of labor. A strong and very painful contraction may be followed by a mild and weak one; or, one or two weak pains may precede a very firm and painful one. The periods of lessened work and the phases of complete relaxation and rest between contractions are no doubt useful for the carrying off of the waste products of muscular activity by the circulatory system, and for supplying the fetus with sustaining oxygen and the uterine tissues with fresh oxygenated blood in preparation for the exertion.

Figure 7 is the reproduction of a tracing made by the contraction of the uterus of a primiparous patient, who had had no agents

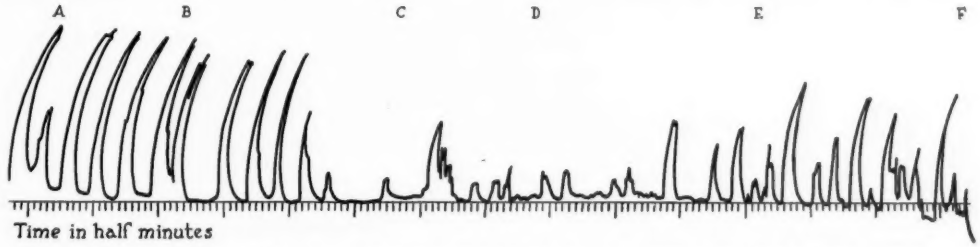

Fig. 13. Tracings of a typical low forceps delivery; ether anæsthesia; primipara. *A*, Cervix fully dilated; *B*, head on perineum; *C*, ether on, to control contractions; *D*, scrub; *E*, delivery begun—left occiput anterior presentation, low forceps, no ether for contractions; *F*, birth.

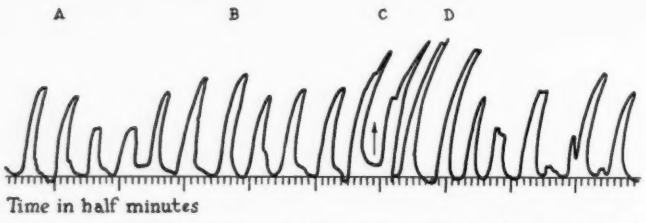

Fig. 14. The effect of nitrous-oxide-oxygen analgesia. Primipara; cervix dilated two and one half fingers. *A*, No inhalation analgesia; *B*, contractions painful; *C*, nitrous-oxide analgesia; *D*, patient comfortable.

for the relief of pain. The cervix at the time this study was made was dilated 7 centimeters and the fetus was presenting in the left occipitoposterior position. One can observe that the intervals between the several contractions vary from ½ minute to 3 minutes; that there is a variation in the degree of intensity between certain of the several contractions, that two and possibly three double contractions occurred; and that the duration of time from the beginning of the increment to the end of the decrement varies in different contractions from less than 1 minute to nearly 3. It is also remarkable that although the contractions may reach their maximum slowly, they do not always do so gradually; an occasional one seems to maintain iself at a certain level for a short period of time, and then suddenly increases in intensity. The impression made by the movement of a fetal small part is also apparent in this exhibit (the quick contraction fifth from the right).

The contractions of the uterus in labor are not painful throughout the entire phase. For a very short time after the contraction begins there is no sensation of pain, and shortly before complete relaxation has been reached pain disappears. Pain becomes progressively more severe from its onset and is maintained at its peak during the entire acme of the contraction, leaving gradually as the uterus relaxes. The letters *A* and *B* in Figure 8 indicate, respectively, the points on the tracing where pain was first experienced and where it entirely disappeared. These were analogous for all of the contractions shown. This particular tracing also demonstrates, in contrast to the one discussed in the preceding paragraph, the longer periods of time which may be consumed from the beginning to the end of contractions. Here the periods extend from 1 minute to 3 minutes, while the intervals range from less than a minute to over 3. The individual variations in the intensity of the contractions, too, as well as fetal movements and a "double pain" are evident here.

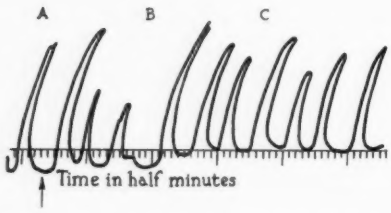

Fig. 14 A. *A*, Nitrous-oxide, surgical depth, begun; *B*, patient completely anæsthetized; *C*, note increased tonicity.

The uterine forces in the first stage of normal unobstructed labor perform among others, two main functions: the dilatation and effacement of the cervix. During this period the patient herself plays a more or less passive rôle, in that she is unable to help the course of labor to any great extent. When the cervix is fully obliterated and opened, however, the pains take on an expulsive character. The patient becomes aware of a body in her pelvis —the presenting part of the fetus—and she experiences a desire to expel it. Then, with the onset of each pain, she fixes her diaphragm and chest in inspiration, closes the glottis, and by a powerful and rigid action of the abdominal muscles "bears down" or strives to drive the presenting part to a lower plane in the pelvis, or onto the perineum. The patient often makes several expulsive efforts, similar to the one described, throughout the

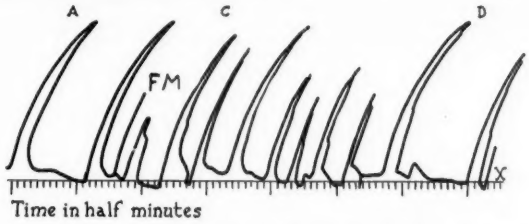

Fig. 15. Note the severe and strong contractions recorded before the administration of spinal anæsthesia. Patient was a primipara, left occiput posterior presentation, cervix 9 centimeters dilated. *A*, Contractions severe; *FM*, fetal movements; *C*, patient complains bitterly. *D*, 2 cubic centimeters spinocain were injected between fourth and fifth lumbar vertebræ at *x*.

duration of a single contraction while the uterus remains firm.

Graphically the transition which occurs from the first stage to the second is most vivid. From the even and smooth curves seen nearly always in the first stage, the tracings reveal lines superimposed upon the basic curve of the contractions in second stage labor. These accessory lines are due to the several expulsive efforts of the patient which increase the intra-abdominal pressure.

Figure 9 very clearly shows this transition at the time of complete effacement and dilation of the cervix. The case represented is that of a primiparous patient, who had not been given any analgesia or anæsthesia so that an uninfluenced record might be made. At point *B* on the tracing the curves begin to take on the few accessory superimposed tracings of early second stage labor, and from 7 minutes after that point all of the subsequent contractions are accompanied by "bearing down" efforts. Due to the fact that the graph paper moves slowly (at a rate of 1 inch every 5 minutes) the semi-voluntary expulsive and "bearing down" tracings come very close together, and individual lines may be obscured by the proximity.

With my method of recording the tracings described above are typical of the second stage when no anæsthetic has been administered, and Figure 10 demonstrates a 25 minute period following complete dilatation of the cervix in a primiparous patient.

A Classification of the Agents Studied

The medicaments and agents generally used during the first and second stages of labor can, broadly speaking, be divided into two main groups: (1) those which are used to relieve suffering and mental anguish so that labor may be bearable during its entire course; and (2) those which are used to stimulate the progress of labor so that the period of time during which a patient must suffer will be shortened. The first are given primarily

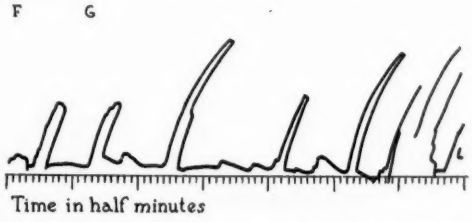

Fig. 15A. The immediate effect of spinal anæsthesia. Depression of frequency and intensity; increased tonicity. The base line is higher than in Figure 15. *F*, Immediately after completion of intraspinal injection; *G*, patient feels no pain during uterine contractions; and is completely anæsthetic caudal to the costal margin.

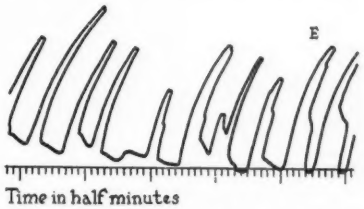

Fig. 15B. Anæsthesia persists but contractions recur. Tonicity of uterus approaching complete relaxation between contractions near the end of the tracing. *E*, Anæsthesia persists and continued in all for 1.5 hours.

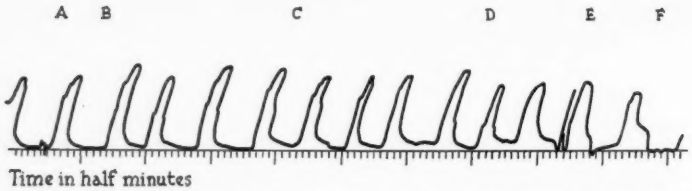

Fig. 16. The immediate effect of ¼ grain morphine on the uterine contractions in early labor. Depression of frequency and intensity; increased tonicity. Patient was a primipara; cervix dilated one half finger, vertex presenting. *A*, Contractions very painful, patient very restless; *B*, contractions of long duration; *C*, morphine sulphate, ¼ grains, hypodermatically; *D*, patient beginning to feel sleepy; *E*, patient sleeping between and during contractions, groans a bit during pains; *F*, duration of contractions increased, intensity somewhat less.

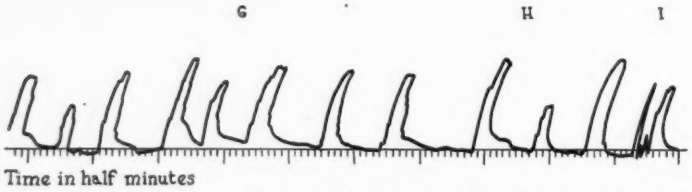

Fig. 16 A. From 30 minutes to 80 minutes after morphine. Compare with Figure 16. Note the increased intervals and prolonged decrements. *G*, Patient resting completely during and between pains; *H*, patient somewhat restless, but not awake, during contractions; *I*, fetal movements.

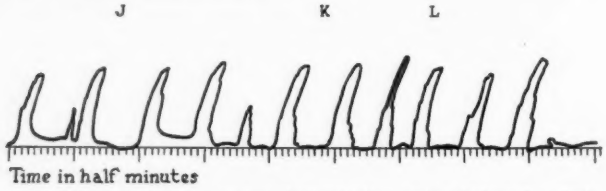

Fig. 16 B. The tracings appear similar to those taken before the administration of morphine (Fig. 16), 85 to 125 minutes after administration. *J*, Patient becoming somewhat wakeful and complains very little during contractions; *K*, cervix one and a half fingers dilated; *L*, contractions arouse patient.

where the patient's welfare and comfort are considered, and the second for bringing matters to a crisis. In a well managed labor, combinations of drugs from both groups may be called into use according to the conditions surrounding each individual case.

The agents with which this study is chiefly concerned are classified as follows:

Group I

1. Anæsthetics
   a. General administration—ether, nitrous-oxide-oxygen.
   b. Regional, or intra-spinal administration—spinocain[1].
2. Analgesics
   a. Hypodermic administration—morphine sulphate, morphine and scopolamine
   b. Rectal, or Colonic administration—"Gwathmey mixture No. 2[2], "Gwathmey mixture No. 3[3], "avertin fluid"[4]
   c. Oral administration—"sodium amytal"[5]

Group II

3. Oxytoxics
   a. Hypodermic administration—pituitary extract, "thymophysin"[6]
   b. Oral administrations—quinine sulphate.

[1] Spinocain (Metz). Each 2 cubic centimeter ampule contains 200 milligrams novocain; 2.2 milligrams strychnine sulphate, in a special solution; alcohol 14.5 per cent.

[2] Gwathmey mixture No. 2 contains oz. iiss; alcohol 3 drams, quinine hydrobromide 10 grains; liquid petrolatum, qs. ad. oz. iv.

[3] Gwathmey mixture No. 3 same as above without quinine or alcohol.

[4] Avertin fluid, solution tribromethanol (Winthrop).

[5] Sodium amytal, sodium iso-amyl-ethyl barbiturate (Lilly).

[6] Thymophysin, a non-standardized combination of pituitary and thymus extracts—Temesvary (American Bio-Chemical Laboratories).

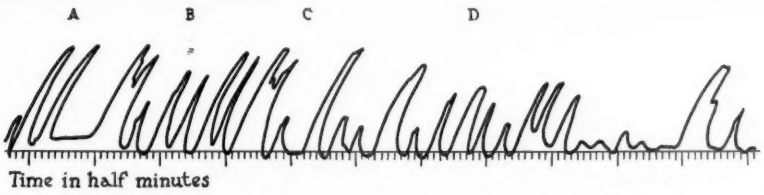

Fig. 17. Tracings showing the immediate effect of morphine scopolamine upon the uterine contractions in a primiparous patient. *A*, First stage, two fingers' dilatation, no analgesia or anæsthesia; *B*, patient complaining and very restless; *C*, $^1/_6$ grain morphine, $^1/_{150}$ grain scopolamine; *D*, sleeping, no complaints during contractions.

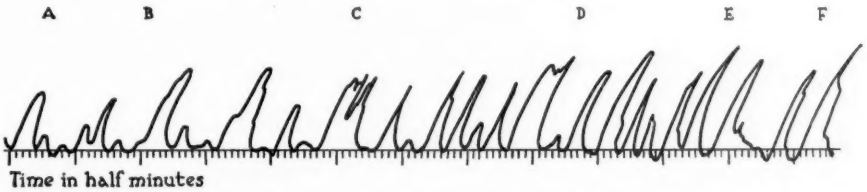

Fig. 17A. Tracings showing the effect of two subsequent injections of scopolamine in the same patient as in Figure 17. *A*, Injection of $^1/_{90}$ grain scopolamine; *B*, patient groaning during contractions, sleeping well between pains; *C*, restless during pains, restful between pains; D, scopolamine injection of $^1/_{400}$ grain; *E*, very restless during pains, sleeps between contractions; *F*, rectal ether given.

In Group I are found that invaluable class of agents—the anæsthetics and analgesics—which when skillfully used, and wisely, can be made to transform what is too often a horribly painful, exhausting, and tortuous ordeal into nothing more than a vague memory of an uncomfortable experience. At the Cleveland Maternity Hospital, certain anæsthetics and analgesics, after a long period of clinical observation, have come to be used more or less routinely; and for the purpose of confirming or altering the clinical impressions which have been gained as well as for the purpose of studying the action of several less extensively used, and consequently less familiar preparations, this investigation has primarily been undertaken.

The Influence of the Agents Upon the Uterus in Labor

Ether. Sir James Y. Simpson was the first to use ether in obstetric practice on January 19, 1847, when he did a version and extraction (De Lee). In the United States at the present time, ether is probably used at the time of delivery to a greater extent than any other anæsthetic. Because of the safety with which it can be administered, its hypnotic and anæsthetic effects upon the patient, and the property which it has of depressing the intensity and frequency of the contractions of the uterus, ether can be regarded as an invaluable drug not only in unobstructed labor but particularly in the dystocias which are terminated vaginally.

One may control the contractions of the uterus with ether, at will. In direct proportion to the depth to which this anæsthetic is administered are the intervals between contractions prolonged and the intensity decreased; and they can be entirely obliterated when the concentration of ether has reached the surgical degree. Conversely, as the ether absorbed by the patient is eliminated, the contractions begin to recur and increase in intensity and frequency at about the same rate at which they were decreased. This property of ether is often a life saving virtue, as when rapid intra-uterine manipulations must be carried out; when excess uterine pressure is being exerted upon the fetus; when a contraction ring must be relaxed; when the danger of rupture of the uterus is imminent due to a weak hysterotomy scar or to the

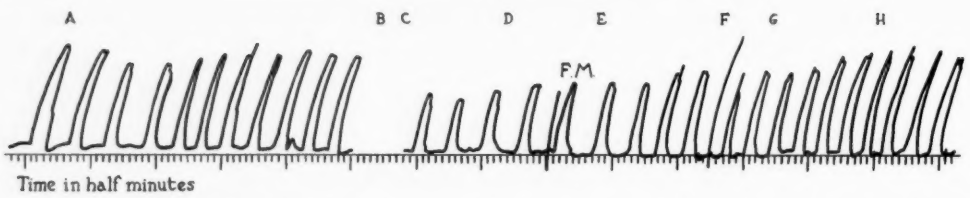

Fig. 18. The effect of colonic ether with quinine upon the contractions of the uterus. Patient was a primipara; cervix was two and one-half fingers dilated; vertex, left occiput anterior. *A*, Patient restless and uncomfortable, during and between pains; *B*, colonic ether instillations, 2 ounces with 10 grains quinine; *C*, 15 minutes after instillation; *D*, patient comfortable and does not complain or become restless; *FM*, fetal movements; *E*, intervals between pains greater and intensity decreased; *F*, cough; *G*, contractions becoming more frequent and intense, but patient is sleeping; *H*, contractions similar to those before instillation, patient comfortable.

inadvised administration of an oxytoxic; as well as when many other conditions may arise where labor must be stopped.

Figure 11 demonstrates most conclusively the effect which ether has. The tracing represents a multiparous patient who at the point *A* is entering the second stage of labor. She has been allowed to have three second stage contractions (characterized by the superimposed tracings of additional abdominal pressure) before ether was begun. The first effect of the ether is to remove the semi-voluntary "bearing down" efforts, at point *B*; then to decrease the intensity of the contractions and finally to obliterate them almost entirely.

Ether is also very satisfactorily used for its pain alleviating qualities alone—as an analgesic. When given in approximately 1 dram doses, in a partially dosed mask or cone at the beginning of each contraction, the sensation of pain is almost entirely removed, and the progress of labor is not impaired. Figure 12 is a tracing of a patient similarly treated, and no influence upon the force or frequency of the contractions is noticeable.

When ether is used as an analgesic, the depth at which it is being given can be increased, so that as the time for delivery approaches the patient is anæsthetized. At the Cleveland Maternity Hospital this method is used almost to the exclusion of any other. When the patient is ready to be delivered, she is anæsthetized to the extent that the uterine contractions are almost entirely obliterated, so that the preparation of the field of operation may be carefully done and the perineum well dilated manually. In the event the delivery necessitates some intra-uterine manipulation as in podalic version and extraction, or simple extraction for breech presentation, the anæsthesia is continued until these maneuvers are completed. However, if the patient is to be delivered with forceps the ether is removed after the forceps are applied so that the contractions may recur. Traction on the forceps is made then with each contraction. When the head is brought down to that plane in the pelvis where the chin can be felt through the perineum, the forceps are removed and the anæsthesia reinforced. The head is thus delivered under the complete control of the operator, and he may extract it slowly and with care, preserving the perineum to the greatest extent. Figure 13 represents a tracing of a typical low-forceps delivery with ether anæsthesia, in a primiparous patient.

Nitrous-oxide-oxygen gas. Priestly, about 1776, first prepared this gas, and its anæsthetic properties were first described by Humphrey Davy and by Wells. Edmund Andrews, of Chicago, in 1868 was the first to administer it combined with oxygen, as a safe and satisfactory anæsthetic (Sollman, Luckhardt).

When nitrous-oxide-oxygen is administered during labor, it acts purely as an anæsthetic or analgesic, with no depressant effect upon the contracting uterus. I have been unable to cause any cessation or diminution of the frequency or intensity of the contractions regardless of the depth to which the gas had been administered. On the other hand, several of the tracings bear out the contention that

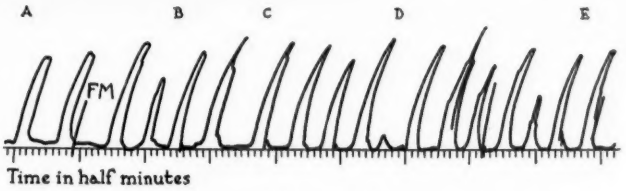

Fig. 10. Normal contractions, first stage of labor in a primiparous patient; cervix dilated four fingers; left occipito-anterior position. *A*, Patient very uncomfortable, effect of morphine and scopolamine wearing off; *FM*, fetal movements; *B*, contractions painful; *C*, patient restless; *D*, patient in need of further analgesia; *E*, cervix fully dilated.

this gas may even stimulate or increase uterine contractions. Other investigators have made the same observations (Danforth and Davis).

At *C* in Figure 14, nitrous-oxide-oxygen gas was started and given continuously. The patient was not completely unconscious during this period but the concentration of gas was sufficient to remove all sensation of pain. The contractions continued at approximately the same frequency with a noticeable tendency to an increase in intensity. At *A* in Figure 14A (the same patient) the concentration of the gas mixture was increased so that 10 minutes later the patient was completely anæsthetized. The contractions continued at the same frequency. At the point where complete anæsthesia occurred the tonicity of the uterus was greatly increased, evidenced by the rise of the base line, and the contractions became more regular. Although the patient showed no external evidence of asphyxia it probably occurred to a certain degree in the uterine tissues, causing the slight incomplete tetany—the incomplete relaxation phases. The palpating hand, alone, would not be able to determine this change, and it is therefore important to realize that a fetus may be subjected to increased pressure and be deprived of a certain amount of oxygen exchange, when nitrous-oxide-oxygen gas is administered for any length of time to more than an analgesic degree.

Internal podalic version, the decomposition of a frank breech presentation into a footling, or even the manual removal of an adherent placenta, can not be safely or conveniently done under this anæsthetic. The reasons are apparent.

Spinocain. The use of spinal anæsthesia in obstetrics has had its days of enthusiasm and its days of derision, and today there are reports which deny the dangers and complications which other reports charge, accompany its use. With the possible exception of satisfactory local anæsthetic infiltration, the consensus of opinion seems to favor the use of spinal anæsthesia for abdominal delivery where respiratory, cardiac, or systemic contraindications to general anæsthesia exist, just as in general abdominal surgery.

For the delivery of women vaginally, there seems to be a general appreciation of the unreliable action of the spinal anæsthetic (DeLee and Greenhill, 10) upon the tonicity of the uterus and cervix, in addition to the effect which the drugs used may have upon blood pressure, blood loss, and the nervous system. Shock and collapse also occur now and then, and vomiting is sometimes a complication.

Whitehouse and Featherstone, in 1923, described the effect upon the uterus of injecting tropacocaine into the spinal cord with the following: "When the lumbar cord is paralyzed by the drug, the uterus always

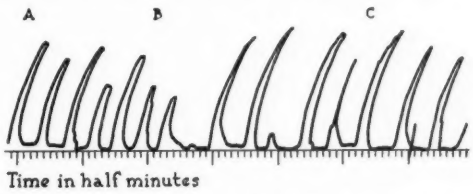

Fig. 19 A. Contractions of the uterus after colonic instillation of ether without quinine. (Compare with Figure 19.) *A*, Fifteen minutes after administration of colonic ether, 2 ounces without quinine; *B*, patient sleeping during and between pains; *C*, patient apparently very comfortable.

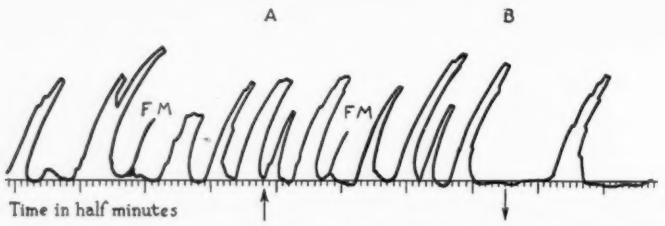

Fig. 20. Normal contractions before the rectal instillation of avertin. Primipara, first stage; no analgesia or anæsthesia. *FM*, Fetal movements; *A*, three fingers' dilatation; *B*, avertin given per rectum, 60 milligrams per kilogram.

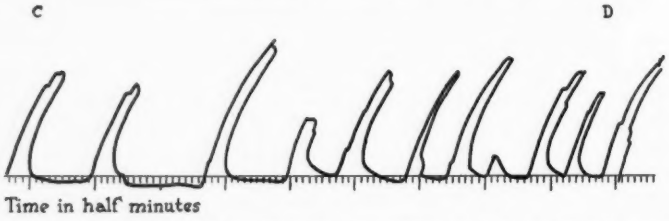

Fig. 20 A. The effect of avertin upon the contractions is to prolong the intervals. (Compare with Fig. 20.) *C*, Patient asleep; *D*, patient becoming restless, less than 1 hour after avertin; four fingers' dilatation.

contracts and it does not relax until the drug ceases to act." Metzger, since that time, concluded that the injection of 0.7 cubic centimeter of a 10 per cent solution of stovaine provoked a hypertonicity of the uterus, and Bourne and Burn conclude that stovaine intraspinally does not inhibit the contractions of the uterus but interferes with complete relaxation between pains.

On the other hand, J. W. Kelso says that caudal anæsthesia produces a certain amount of inertia of the uterus in practically every case, while Henry and Jaur report that if epidural anæsthesia is given too high there is danger from uterine hæmorrhage due to inertia and that in the low type there is no uterine anæsthesia.

For the purpose of study we have injected "spinocain" intraspinally and have recorded the contractions of the uterus before and after. Figure 15 represents the contractions of a primiparous patient (9 centimeters dilated) before 2 cubic centimeters of spinocain were injected, at point *x*. Figure 15A represents the immediate uterine reaction—a diminution in the frequency and in the intensity of several contractions for a period of 30 minutes before they resumed their previous character; and a rise of the base line, indicating relaxations to a less degree than before the intraspinal injection. The increased tone persisted for 45 minutes until, in Figure 15B, the relaxations between contractions seemed to fall to the original base line.

The patient was free of labor pains for nearly 2 hours after the injection, the region of anæsthesia extending from the costal margins. However, the cervix was not completely dilated until nearly 4 hours after the spinal injection and ether inhalations had to be given to alleviate the recurring pain. It is interesting to note in this case that when delivery was attempted, the vertex was found to be in the left occipitoposterior position and above the brim of the pelvis and that attempts to deliver by internal podalic version were frustrated by a tonic uterus. Laparotrachelotomy was resorted to. The patient made an uneventful recovery and the condition of the baby was good.

Morphine. Clinical experience with the administration of morphine during labor indicates that the action of that drug is not always the same. Upon some patients it

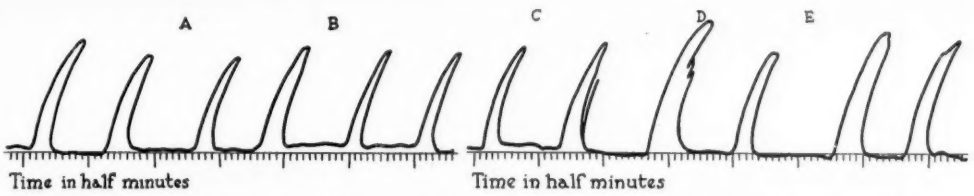

Fig. 21. The regular contractions of the uterus during labor of a multiparous patient, in first stage; no analgesia or anæsthesia. *A*, Contractions painful; *B*, patient restless.

Fig. 21 A. Tracings demonstrate no immediate effect upon the contractions of the uterus after the oral administration of sodium amytal, 12 grains. *C*, 12 grains sodium amytal was given by mouth; *D*, contractions harder; *E*, patient sleeping soundly between contractions, is only very slightly restless during pains.

occasionally has the effect of hastening labor; in others it may have no effect upon the progress of labor; in another group it may retard progress for a very short time; and in nearly all patients it affords temporary relief from suffering.

Generally, experimental evidence regarding the action of this drug upon the contractions of the uterus in labor pretty well fits in with Hensen's opinion, that in moderate doses morphine has little or no effect. Rucker (29), however, demonstrated a tracing made by internal hysterography, in which there was decided diminution in the frequency of the contractions after the hypodermic administration of 1/6 grain of morphine; and at the same time called attention to the clinical fact —often observed in practice—that an increase in uterine contractions may follow a small dose of morphine.

In animals morphine has no effect upon the normal contractions of the uterus *in situ*, but when applied to the excised uterus, the tone is somewhat increased (Sollmann, Barbour; Barbour and Copenhaver).

The several observations which I have made upon the human uterus in labor after the administration of morphine agree with those made by the investigators quoted above. In addition I also have tracings which would seem to agree with the results of Bourne and Burn (5) who say: "Morphine lessens the frequency of uterine contractions, but the pains pass off more slowly."

These writers assume, however, that since the contractions pass off less quickly than before, the work done by the uterus is probably as great or even greater than before, despite the lessened frequency. I believe that this conclusion is not soundly based, since it is not the tightly contracted organ which is of value, from the mechanical standpoint, but that it is the period of increase, or increment of the contraction, which is effective.

Figures 16, 16A, and 16B illustrate the average effect of 1/4 grain of morphine upon a primiparous woman in early first stage labor. Fifteen minutes after the administration of the drug, hypodermically (Fig. 16), the patient began to feel sleepy and for the next 15 minutes the intensity of the contractions appear to have been lessened to a slight degree, although the time intervals of recurrence are maintained. For the next 45 minutes (Fig. 16A) the contractions again reach their former intensity but the intervals between them are very slightly prolonged, and the periods of relaxation for each individual contraction are increased. Thereafter, the tracings return to their appearance before the administration of the narcotic. It is most noteworthy that not only did the patient have an almost complete rest for over 1½ hours, from the effect of the morphine (and at the end of that time she was merely aroused by

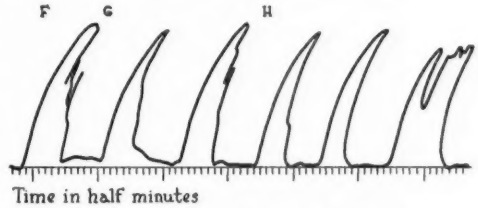

Fig. 21 B. *F*, One hour and forty-five minutes after sodium amytal was administered. Contractions regular and forceful, patient comfortable. *G*, Contractions more frequent and stronger; *H*, patient sleeps very soundly between pains. Moves about with pains.

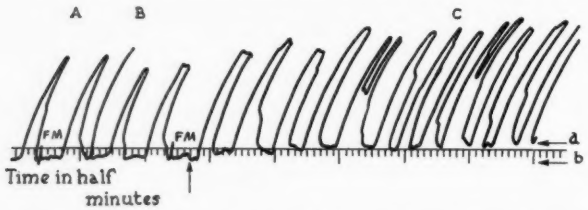

Fig. 22. The action of 3 minims of pituitary extract upon the first stage contractions is to increase the force, frequency, and tonicity of the uterine contractions. Secundipara, vertex at low mid, left occipito-anterior. *FM*, Fetal movements; *A*, three and one-half fingers' dilatation; *B*, cough; arrow indicates injection of 3 minims of pituitrin; *C*, cervix near full dilatation.

the contractions) but that labor progressed, the cervix dilating from approximately 1 centimeter to 3 centimeters.

Since morphine has no marked or prolonged depressing effect upon the uterine contractions of an established labor, it is often used as a test to differentiate true from false labor. Almost invariably morphine will stop the contractions of the uterus when labor is false.

Reference was made in a preceding paragraph to the occasional clinical effect of morphine—its stimulating action. Often a patient who has been in labor for some time and has made little or no progress, is given a hypodermic of morphine, and shortly thereafter the cervix is completely opened and delivery may follow at once. This reaction is probably due to a combination of the relaxation of the cervix, an increased tonicity of the uterine muscle, and a general refreshment of the whole organism resulting from induced psychic tranquility.

Morphine and scopolamine. In 1901, V. Steinbuechel (34) first used morphine and scopolamine in obstetrics, and Gauss and Kroenig's clinical use of this combination in the University Women's Hospital of Freiburg is well known. The first years of the combined use of these drugs were limited to Europe, and after a wave of enthusiasm in the United States subsequent to that time, it was more or less abandoned as a routine analgesia in labor. However, in a few clinics in this country, at the present time, "twilight sleep" analgesia is used, but the method is a modification of the original Freiburg method (De Lee). For two decades the use of morphine and scopolamine has been routine for primiparous patients in the Cleveland Maternity Hospital, and there has never been any question of discontinuing its use (Bill).

On the basis that if given too close to the time of delivery it may cause depression of respiration in the baby, the treatment is not started when delivery either vaginally or abdominally is expected within 4 hours. Other than for this contra-indication, morphine and scopolamine are never denied a patient.

As soon as a primiparous patient begins to complain of pain or discomfort she is given 1/6 grain morphine and 1/150 grain scopolamine hypodermically. Forty-five minutes later a hypodermic injection of 1/200 grain of scopolamine is given to be followed in another 45 minutes by 1/400 grain of the same drug. From that time on she receives every 1½ hours, subsequent doses of 1/400 grain until it is estimated that the patient will be ready to be delivered in 3 to 4 hours. Occasionally a dose of scopolamine during the course will be combined with an additional dose of morphine 1/6 grain, if the course of labor is unusually slow, or if the patient seems somewhat restless. Amnesia is complete in the greatest majority of patients, and once in a while a patient may recall some unimportant incident concerning her care or an examination; but there is no memory of pain.

Since delivery of a patient usually occurs within 2 to 2½ hours after the beginning of second stage labor, the injections of scopolamine are stopped when the cervix is dilated about 8.5 centimeters and analgesia is continued by inhalations of ether or nitrous-oxide-oxygen, or a colonic instillation of

ether. If the morphine-scopolamine routine is carried out with due regard for the time of expected delivery, no baby suffers any respiratory depression from the drugs. If a baby does have simple asphyxia at the time of delivery, the delay in respiration is not due to the hypodermic analgesia, but rather to its having absorbed a share of the general anæsthesia which made the mother unconscious. Gentle manipulations invariably start respiratory efforts, and regular normal breathing follows immediately thereafter.

Scopolamine combined with morphine has no characteristic effect upon the uterus in labor, other than that which is seen from morphine alone. Just as morphine generally does not interfere with the normal progress of labor to any appreciable degree one way or the other, so is it when the treatment described at length above is given. Figures 17 and 17A give a fair idea of the usual effect.

In the first series (Figs. 17 and 17A) there is somewhat of a depression in the intensity of several of the contractions following the initial dose, but labor continued. After the effect of this hypodermic injection seemed to have worn off—a period of about 45 minutes—the contractions assumed their previous degrees of intensity, despite subsequent administrations of scopolamine alone. The patient was relieved of all mental anguish and whatever suffering she may have had was manifested only by her restlessness during contractions as labor advanced.

Gwathmey mixture No. 2. On May 11, 1923, James T. Gwathmey, M.D., et al., with a vision toward an ideal, presented a preliminary report before the Atlantic City Medical Society, entitled, "Painless Childbirth by Synergistic Methods" (14). This was the first chapter in the history of what has now become a nationally known and widely used method for alleviating suffering during confinement. It has no doubt been one of the better contributions in the way of a safe and almost "foolproof" analgesia for general use in obstetrics, since the beginning of this century. His recent report (13) including a study of more than twenty thousand cases, proves conclusively the value of the method in general obstetric practice.

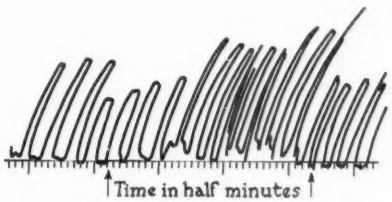

Fig. 23. These tracings represent the effect of thymophysin—Temesvary—upon the uterus in labor. Note the increased frequency, intensity, and tonicity, and compare with Figure 22. Patient was a ii-para, cervix was dilated three and one-half fingers, presentation was right occipito-anterior. The first arrow indicates the injection of 7 minims of thymophysin; the second arrow, beginning relaxation.

The Gwathmey technique (8) is not followed implicitly in the Maternity Hospital of Cleveland, but the ether-oil colonic instillation, somewhat as he describes, is very often used as a supplementary analgesia in primiparous patients who are being carried on morphine-scopolamine, and in multiparous cases, combined with the oral administration of "sodium amytal."

The mixture No. 2 which we use is composed of 2.5 ounces of ether, 3 drams of alcohol, quinine hydrobromide 10 grains, and sufficient liquid petroleum to make a 4 ounce mixture. This mixture is used by us very often, and its effect when administered rectally has a profound tendency, in most instances, to give the patient relief from pain and to cause sleep for varying lengths of time. Its effect upon the contractions of the uterus are almost nil, and are so slight as to be ignored, although there may be a period of from 5 to 10 minutes after the administration of the mixture in which the contractions are slightly decreased in intensity. But this very slight *prolongation* of labor is certainly compensated for in the comfort of the patient.

Figure 18 is typically representative of what happens to the contractions of the uterus after a colonic instillation of ether-oil, containing quinine.

Gwathmey mixture No. 3. This mixture does not contain any quinine or alcohol and is occasionally used by us in any case where possible stimulation of the uterus is to be avoided, as in patients who have had previous cæsarean sections, or where the contractions are already extremely intense and recur very

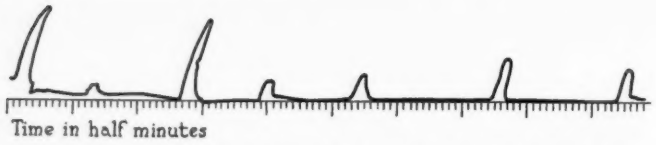

Fig. 24. "False" labor pains induced in a primipara at term, by the administration of 10 grains of quinine sulphate orally. Quinine had been given 20 minutes before starting tracing. Patient was delivered after a period of complete cessation of contractions about 72 hours later.

often. Although the effect of quinine upon the uterus, in labor, is said to be one of stimulation, it is well known clinically that it actually fails in many instances. However, this drug is excluded, for theoretical if not for practical reasons, in the conditions already mentioned.

There is only a very little contrast between the tracings taken where quinine was included and where it was excluded in the colonic instillations.

Figure 19A illustrates the tracings recorded upon a primiparous patient for 35 minutes beginning 15 minutes after a colonic instillation of ether without quinine. Very little if any marked difference can be seen in these tracings and those of Figure 19, taken over a period of 50 minutes before the analgesia was given.

Avertin, tribromethanol, or avertin fluid, which has had a rather wide usage in Europe as a rectal anæsthetic for surgical cases, has been recently used in the United States in weaker concentrations for obstetrical analgesia. All reports regarding its value are not equally enthusiastic but most of the writers agree that close watch must be kept for evidence of respiratory depression and lowered blood pressure.

Deaths due to this drug have been reported in the literature, but Naujoks believes that not all of them were due to the drug itself but rather to excessive doses or faulty technique. The important thing, however, is that deaths have followed its use.

Avertin does produce anæsthesia, and in smaller doses, analgesia, but as Barlow et al., of Western Reserve University, have pointed out in their experimental study of the preparation, in rats, the duration of the maximal action is quite limited. It is, therefore, best given in general surgery as a preliminary to a fortifying general or local anæsthesia; and given in obstetrics, in concentrations not so great, as an analgesia at the end of the first stage, with a general anæsthetic for delivery.

I have found that avertin given by rectum in the proportion of 60 milligrams per kilogram of body weight—the recommended concentration for obstetrical analgesia—has no marked influence upon the contractions of the uterus other than to prolong greatly the intervals between them for about 45 minutes after the administration. During this period, the patient is usually very quiet and sleeps, but very frequent observations are made of her blood pressure and respiratory rate during the first 25 to 30 minutes of this period of rest. When the effect of the medication begins to wear off at the end of 45 to 50 minutes following its administration, the uterine contractions resume their former frequency and painfulness, and the patient becomes restless, occasionally unmanageable. Inhalation analgesia is invariably resorted to in order that the patient may be kept comfortable.

Although this preparation does produce satisfactory analgesia there seems to be nothing to recommend its use when compared with the rectal instillations of ether-oil mixtures for the same purpose. As a matter of fact, comparison highly recommends the latter. Avertin when given in a comparatively harmless dose gives a period of analgesia and rest which at its best does not extend over 45 to 50 minutes, whereas the Gwathmey mixtures produce a period of rest and relaxation free from pain for an hour as an average and a subsequent period of from 30 minutes to an hour of comfort. Uterine contractions are interfered with to a less degree by colonic ether-oil instillations and it is unnecessary to take special precautions for the safety of the patient's

Fig. 25. The possible effect of the administration of quinine sulphate upon the labor of a primiparous patient. Some increase in frequency and intensity of the contractions is noted 15 minutes after the drug was given, which action may have been due to the drug. *A*, Cervix three fingers dilated, patient had had no analgesia or anæsthesia; *B*, contractions very painful; *C*, quinine sulphate, 10 grains; *D*, patient restless; *E*, patient very uncomfortable.

general condition. Avertin should only be given when ample assistance is available in case untoward reactions occur, and equipment for carbon-dioxide-oxygen administration should be at hand. A patient can not be left in the care of any one other than an anæsthetist or very well trained nurse assistant after the administration of avertin, but a student nurse can easily be trusted with the welfare of a patient after colonic ether-oil.

An examination of Figures 20 and 20A will reveal a prolongation of the intervals between the contractions after the instillation of avertin, as compared with those before the drug was given.

Sodium amytal. Doctor Bill suggested the oral administration of sodium iso-amyl-ethyl barbiturate, or "sodium amytal Lilly," in 3 grain units, for multiparous patients, at the Cleveland Maternity Hospital, about 2 years ago. The analgesia and amnesia which this drug produced during the first stage of labor in doses from 9 to 15 grains was most gratifying and its use is now a regular part of the analgesia routine for multiparæ. Combined with colonic instillations of ether-oil, patients are very satisfactorily carried through the greater part of the first stage of labor. With inhalation anæsthesia for delivery, childbirth and confinement becomes practically painless for the multipara to whom one might hesitate to give morphine hypodermically because of the uncertainty of the time of delivery with consequent respiratory depression of the baby.

Soon after she is admitted, the multiparous patient is given 9 grains of the drug by mouth, and within 15 to 20 minutes the patient is usually sound asleep and may not even stir during contractions. The average patient rests from 1½ to 2½ hours with this dose, and when sleep becomes light a subsequent dose of 3 to 6 grains may be given without hesitancy. Whenever it is considered desirable, ether-oil is given by rectum, and there are no contra-indications to the combination of these two preparations except those local conditions of the descending colon and rectum which preclude the ether-oil.

There has never been any apparent danger to the baby from sodium amytal, but very occasionally a patient has become excited rather than tranquil from its use. In the latter cases, ether-oil by rectum (which may be repeated in 3 to 4 hours) usually suffices to quiet the patient.

Sodium amytal has absolutely no depressing effect upon the contracting uterus in labor, nor does it have any tendency to interfere with complete relaxation of the uterine musculature in the intervals between contractions. On the other hand, the drug seems to cause a very desirable relaxation of the lower uterine segment. Dilatation of the os is, therefore, often more rapid than would ordinarily be expected, and for this reason the contractions often become more intense—but not painful—under the influence of this hypnotic.

The series of tracings in Figures 21, 21A, and 21B are most interesting. In the first is represented the regular painful contractions of the first stage of labor in a secundipara, who had had no medicaments for the relief of her suffering. At point *C* in Figure 21A, 12 grains of sodium amytal were given by mouth. Despite the fact that the contractions became

more intense, the patient was soundly sleeping in less than 20 minutes, moving about somewhat but not complaining during the contractions. One hour and forty-five minutes later (Fig. 21B) the patient was still asleep between contractions and stirred only during them. There was still no evidence of suffering 2 hours and 20 minutes after the drug had been given, when the tracings were discontinued. It is most apparent that labor continued uninterruptedly.

Pituitary extract. In 1927, when Bourne and Burn (4) were investigating the dosage and action of pituitary extract before delivery, they found that in nearly half of the primiparous labors which they studied by internal hysterography, the uteri became tonically contracted after the injection of two units of pituitary extract, and the increased tonicity persisted from 10 to 30 minutes.

Rucker (28), in 1925, came to the same conclusion regarding the action of pituitary extract, referring to the incomplete relaxation of the uterus as an "incomplete tetany" and demonstrated tracings which were made by this method of hysterography to substantiate his opinion.

My findings, recorded by external hysterography, concur entirely with those of these investigators. Although the intensity and frequency of the contractions were definitely increased and labor progressed in those cases in which the cervix was dilated from 7.5 to 8 centimeters, the degree of relaxation between contractions was not complete after the injection of 2 to 3 minims of pituitary extract, hypodermically. The period of this increased tonicity averaged about 25 minutes.

With doses as small as those which were used in this study it is not very possible to do a great deal of harm, especially when ether was easily available for administration if it were necessary to retard or subdue tempestuous contractions. However, it is at once most evident that terrific damage might be done if larger doses were injected—(and the literature of the past 16 or 17 years is full of reports of fatal and disastrous results) while the fetus remained *in utero*.

Pituitary extract is a powerful, quickly acting, and tenacious oxytoxic, and although it is of value in isolated instances of uterine inertia during the first or second stage, when administered at intervals of 1 or 2 hours in small doses of 1 or 2 minims by a competent and well trained obstetric surgeon, it is a terrible and dangerous drug when given without regard for its potency or dosage, or maternal and fetal tissues, merely to hasten delivery. Because of the very properties of the drug which contra-indicate its usage almost invariably in first and second stage labor, it is an invaluable addition to the obstetrician's armamentarium during and after the third stage.

Arrow *a* in Figure 22, points to the base line assumed during the intervals between uterine contractions, in a secundiparous patient, after the injection of 3 minims of pituitary extract as compared with the original base line before the injection, indicated by arrow *b*. At the end of 23 minutes, in this tracing the uterus was still in a state of "incomplete tetany" with no indication that it would soon relax.

With these findings in mind, too much stress can not be laid upon the tragic dangers of pituitary extract inadvisedly used; and even in this year of 1932 a word of caution is not amiss.

Thymophysin. With complete regard and respect for the report of the Council on Pharmacy and Chemistry of the American Medical Association which has investigated thymophysin through the research study conducted by Dr. Erwin E. Nelson, of the University of Michigan, the author presents his findings.

The data concerning the exact nature of the preparation was not known at the time these studies were begun, until Nelson's report appeared, but clinical and hysterographic experience with the substance was practically identical with that of pituitary extract.

Nelson concludes that when thymophysin (a mixture of extracts of pituitary and thymus) and equivalent doses of pituitary extract were compared upon excised uteri or on the blood pressure, no differences in action could be demonstrated.

Rucker (30) investigated the action of this mixture upon the pregnant human uterus *in situ* and found that in doses of from 0.5 to 1 cubic centimeter it caused tetanic contrac-

tions similar to the action of pituitary extract, and vigorously condemned it.

Three studies which I made gave recorded tracings very similar to those seen during the investigation of pituitary extracts—an increase in frequency and intensity of the contractions with a lessened degree of relaxation between contractions. Figure 23 is typical after the injection of 0.5 cubic centimeter.

If an oxytoxic with the properties of pituitary extract is desired, let pituitary extract be used. Pituitary extract is standardized, its dangers in first and second stage labor are widely known, and its virtues in third stage labor are recognized. Thymophysin is an unstandardized preparation of varying potency extended to the medical public with glowing promises for its ability to shorten labor safely—and already a case of rupture of the uterus has been reported following its administration.

Quinine. Sollman says that quinine stimulates the contractions and increases the tone of the excised uterus. De Lee (9) gives the percentage as 30 of all cases of women at or near term who begin to have labor contractions after the administration of quinine and says that, during labor, quinine occasionally may aid the weak contractions of an uterine inertia.

Yet it is known clinically that very often quinine has no apparent effect, even when given in repeated doses, and that it may, on the other hand, cause fairly severe increase in tone and intensity of the contractions. Its effect in 10 grain doses, by rectum, has been considered under the discussion of rectal analgesia.

We tried quinine in 10 grain doses in 3 patients at term who had had no labor contractions. In two of these instances there was no stimulation of contractions but, in the third, feeble pains occurred which lasted for about 45 minutes and then subsided completely for 72 hours, when labor started spontaneously (Fig. 24).

Figure 25 represents a typical patient in established labor who was given 10 grains of quinine. A slight increase in the force of the contractions seems to have followed, but with no appreciable effect on the course of labor.

It appears from these few observations, and the observations of others in the clinical-experimental use of quinine in labor, that the powerful effect of quinine upon the excised uterine muscle suspended in a bath is a very unsatisfactory guide to its effect upon the parturient human uterus and that its value in parturition has been overstressed.

SUMMARY

1. A review of the history of methods which have been hitherto used for the purpose of studying the contractions of the human uterus during labor has been made and presented.

2. An original method for external hysterography has been devised and described, whereby tracings of the contractions of the human uterus in labor may be easily and conveniently made during the phase of the first or second stages of labor. This method is entirely harmless so far as the patient or fetus is concerned, and can be satisfactorily applied and used without aid.

3. Tracings have been exhibited, demonstrating the normal first and second stages of labor and their characteristics have been pointed out.

4. The reactions of the uterus during labor and at term to some twelve drugs have been studied graphically to correlate previous clinical impressions with experimental evidence.

5. Ether depresses the contractions of the uterus in direct proportion to the depth to which it is administered, and when given as an analgesic in a semi-closed mask in dram doses it relieves pain but does not retard the progress of labor.

6. Nitrous-oxide-oxygen gas when given either as an analgesic or anæsthetic has no depressant effect upon the contracting uterus. When given to the degree of surgical anæsthesia it may cause an incomplete relaxation of the uterus between contractions, with the consequent possible danger of excess pressure upon the fetus.

7. Novocain, given intraspinally in the form of spinocain causes complete anæsthesia for about 2 hours, with a short period of depression upon the uterine contractions. This

drug induces an increased tonicity of the uterine tissues.

8. The action of morphine sulphate in labor is almost always to give temporary relief from suffering, but the effect upon the contractions of the uterus in established labor is not marked. Occasionally it may depress the contractions for a short time, but it retards labor an unappreciable amount.

9. When scopolamine is combined with morphine the effect upon the uterus is practically the same as with morphine alone. This combination, when given as described, makes an excellent analgesia for primiparous patients, with no ill effect to the mother or to the fetus.

10. The colonic instillation of ether, with and without quinine, has practically the same effect—to give excellent analgesia with a very slight depression of the contractions of the uterus.

11. Avertin, or tribromethanol, given rectally in the dose of 60 milligrams per kilogram of body weight as an analgesic, is unsatisfactory and has no virtues which recommend its use in the dosage mentioned. It does not depress the contractions of the uterus but prolongs the intervals between them; on the other hand, the analgesia does not last sufficiently long to warrant the special care and concern which all patients who have received the drug must get. Many patients become unmanageable when the effect of the drug becomes light. Colonic ether is by far a more superior analgesic for rectal administration.

12. Sodium amytal (sodium iso-amyl-ethyl barbiturate) is an excellent analgesic for oral administration especially in multiparous patients and when combined with rectal ether-oil instillations gives a practically painless confinement and childbirth. It does not retard labor at all in spite of the fact that with from 6 to 12 grains of the drug patients may rest or even sleep from 1 to 3 hours with no discomfort. Its value can not be estimated too highly, and there is no evidence which points to any harmful effect upon mother or child.

13. Thymophysin, an extract of thymus and pituitary, has been considered an unstandardized and unsafe preparation by the American Medical Association and its use to shorten labor has been condemned. Its action is identical with diluted extracts of pituitary and should be entirely avoided. When a powerful oxytoxic is desired, a standardized and known preparation of pituitary gland should be used.

14. Pituitary extract given hypodermically in doses of 2 to 3 minims stimulates the contractions of the uterus in force and frequency but it also causes an incomplete relaxation between contractions—an incomplete tetany—for a period of 20 to 30 minutes. The drug is dangerous when given inadvisedly during the first or second stage of labor.

15. The action of quinine is undependable in labor and late pregnancy but in some cases it has an oxytoxic effect.

REFERENCES

1. Acconci. Sulla contrazione e sull'inerzia dell'utero. Toriano, 1891.
2. Barlow, O. W., Duncan, J. T., Gledhill, J. D. The premedication values of avertin, nembutal, phanodorn and pernocton in relation of nitrous oxide anesthesia. J. Pharmacol. & Exper. Therap., 1931, xli, 367–378.
3. Bill, Arthur H. The choice of methods for making labour easy. Am. J. Obst. & Gynec., 1922, iii.
4. Bourne, Aleck, and Burn, J. H. The dosage and action of pituitary extract and of the ergot alkaloids on the uterus in labour, with a note on the action of adrenalin. J. Obst. & Gynæc., Brit. Emp., 1927, xxiv, 249.
5. Idem. The action on the human uterus of anaesthetics and other drugs commonly used in labour. Brit. M. J., 1930, July 19.
6. Carcassone. Bull. Acad. Imperiale de méd., 1865, xxi, 589.
7. Danforth, W. C., and Davis, C. H. Obstetric anaesthesia and analgesia. J. Am. M. Ass., 1923, lxxxi, 1090.
8. Davis, Asa B. Amelioration of labor pains by morphine-magnesium sulphate injections and colonic ether instillations. Directions for administration by method evolved at the Lying-in Hospital of New York. Surg., Gynec. & Obst., 1925, xl, 863.
9. DeLee, J. B. Obstetrics. 5th ed., pp. 314, 317, 1103. Philadelphia: W. B. Saunders Company.
10. DeLee, J. B., and Greenhill, J. O. Obstetrics. The Practical Medicine Series. Chicago: The Year Book Publishers, 1929, 1930.
11. Doehnoff. Arch. f. Gynæk., 1922, xlii, 305–328.
12. Duncan, Matthews J. Researches in Obstetrics. p. 323. Edinburgh: Adam and Charles Black, 1868.
13. Gwathmey, J. T. Obstetrical analgesia: A further study, based on more than twenty thousand cases. Surg., Gynec. & Obst., 1930, li, 190–195.
14. Gwathmey, J. T., Donovan, E. P., O'Regan, J., Cowan, L. R. Painless childbirth by synergistic methods. Bull. Lying-in Hospital New York City. 1924, xiii, 83–94.

15. HENRY, J. R., and JAUR, L. De l'Anesthesia Epidurale en Obstétrique. Gynécologie et Obstétrique, 1929, xix, 19–33.
16. HENSON, H. Ueber den Einflus des Morphine und des Aethers auf Wehenthatigheit des Uterus nebst Beobachtungen zur Physiologie der Uterus contractionen. Arch. f. Gynaek., 1898, iv, 129.
17. KELSO, J. W. Caudal anæsthesia in obstetrics. Am. J. Obst. & Gynec., 1929, xviii, 415–419.
18. LUCKHARDT, ARNO B. General Anæsthesia. Chemistry in Medicine. p. 451. The Chemical Foundation, Inc., 1929.
19. METZGER, MARCEL. Quelques Observations d'Accouchements Dystociques sous Rachianesthesie. Bull. Soc. d'obst. et de gynéc. de Par., 1928, December, 911.
20. NAUJOKS, H. Zur Bewertung des Avertin. (Avertintodesfall, Avertinexanthem, Avertin bei Eklampsie). Monatschr. f. Geburtsh. u. Gynaek., 1930, lxxxiv, 97.
21. NELSON, ERWIN E. Thymophysin Temesvary. J. Am. M. Ass., 1931, xcvi, 352–356.
22. POLAILLON. Bull. et mém. Soc. de Chir. de Par., 1879, v, 58.
23. Idem. Arch. de physiol., 1880, vii.
24. POULLET. Bull. et mém. Soc. de chir. de Par., 1878, v, 58.
25. Idem. Arch. de tocol., Febrier, 1880.
26. RUEBSAMEN, W. Klinisch-experimentelle Untersuchungen ueber die Wirksamkeit der Wehenmittel in der Nachgeburtsperiode. Muenchen. med. Wchnschr., 1913, lx, 627–630.
27. Idem. Die externe Hysterographie als Klinisch-experimentelle Testmethode fur die Bestimmung der Wertigkeit von Wehenmitteln (Chinin- und Hydreastis-Kotarninpraparate). Arch. f. Gynaek., 1920, cxii, 459.
28. RUCKER, M. PIERCE. The action of pituitary extract on the uterus. J. Am. M. Ass., 1925, lxxxv, 1637–1638.
29. Idem. The action of various anesthetics upon uterine contractions. Current Index Anaes. & Anal., 1926, v, 235–246.
30. Idem. The action of thymophysin on the human pregnant uterus in situ. Am. J. Obst. & Gynec., 1930, xx, 791–797.
31. SCHATZ, FRIEDRICH. Beitrage zur physiologischen Geburtskunde. Arch. f. Gynaek., 1872, iii, 58–144.
32. SOLLMANN, TORALD. Manual of Pharmacology. 2d ed., 267, 548–549, 705. Philadelphia: W. B. Saunders Company, 1924.
33. SUN, KO CHI. Spontaneous contractions of the human uterus. A preliminary report. Bull. Johns Hopkins Hosp., 1925, xxvi, 280–298.
34. VAN HOOSEN, BERTHA. Scopolamine-Morphine Anaesthesia. p. 24. Chicago: The House of Manz, 1915.
35. WESTERMARK, F. Esperimentelle Untersuchungen ueber die Wehenthatigkeit des Menschlishen Uterus bei ber physiologischen Geburt. Skandin. Arch. f. Physiol., 1893, iv, 627–630.
36. WHITEHOUSE and FEATHERSTONE. Certain observations on the innervation of the uterus. J. Obst. & Gynæc. Brit. Emp., 1923, xxx, 565.
37. WILLIAMS, J. WHITRIDGE. Obstetrics. 5th ed., p. 254. New York: D. Appleton and Company, 1926.

HEPATO-LIENOGRAPHY WITH THOROTRAST

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From the Surgical Service of Mt. Sinai Hospital

THE satisfactory roentgenological demonstration of liver and spleen is still an unsolved problem. Though the outline of spleen and liver can sometimes be seen on flat X-ray plates or with the aid of a pneumoperitoneum, no details of structure, either normal or pathological, can be visualized on the films.

Radt[1,2] and Oka[3] have recently advised the intravenous injection of thorium preparations to demonstrate roentgenographically pathological changes in these organs. They found that upon intravenous injections certain colloidal substances are deposited as fine granulæ in the reticulo-endothelial system of the spleen and in the Kupffer cells of the liver. Radt used a thorium-dioxyd solution which is called thorotrast. Thorotrast is prepared by the Heyden Chemical Company in ampuls of 12 cubic centimeters. They have recently made larger ampuls of 25 cubic centimeters each. Thorotrast is injected intravenously on 3 or 4 successive days. The patient is roentgenographed on the fourth or fifth day.

The injections are not followed by any immediate ill effect. No rise of temperature, chill, or vomiting were observed in any of the cases. It is possible, however, that thorotrast may cause harmful late effects, as the major part of the injected substance seems to remain in the liver and spleen more or less permanently.

Before reviewing the clinical results in 6 cases in which thorotrast was used I would like to report on some animal experiments which were performed on rabbits.

Animal 828. Weight 2800 grams. April 1, 1931, 3.2 cubic centimeters of thorotrast was injected into an ear vein. Roentgenogram made April 2 showed both liver and spleen moderately well outlined (Fig. 1). Another roentgenogram, taken on April 4, showed practically identical findings (Fig. 2).

In order to test the maximal toxic dose another dose (5 cubic centimeters) was given to this animal on April 6. The rabbit died during the following night.

Microscopic examination (Dr. Klemperer): There is noted in the spleen (Figs. 3 and 4) a very conspicuous increase of histiocytes which contain brown granules. The granules are apparently also stored in the syncytium, but are absent from the sinus endothelium. The stored histiocytes quite frequently show nuclear damage. The lymph nodes show a storage of brown granules in the sinus endothelium and reticulum. In the liver, the Kupffer cells contain the granules. The liver cells present dark granules which differ in appearance from the colloidal granules.

Conclusions. It cannot be denied that the reticulo-endothelial system shows not only the expected storage of the colloidal material, but also changes of degenerative nature indicated by the nuclear damage. These changes may possibly be due to a toxic dose.

Animal 970. Weight 2600 grams. April 1, 1931, 3 cubic centimeters of thorotrast was injected into an ear vein. X-ray pictures taken on April 2 and April 4 showed only a dim outline of the liver (Fig. 5). The spleen was not visible.

Microscopic findings in the liver and spleen were about identical with those in animal 828. However, the storage in the reticulum was less conspicuous. The lymph nodes were not examined in this case.

Animal 167. Weight 2100 grams. April 4, 4.7 cubic centimeters of thorotrast was injected into an ear vein. An X-ray picture, taken on April 6, showed a very dense shadow of liver and spleen with an excellent outline of both organs (Fig. 6). The animal died on April 22.

Microscopic examination: The intersinusoidal reticulum is crowded with very large phagocytic cells filled with the colloidal material. Nuclear damage is not conspicuous. The sinus endothelial cells do not participate in the storage to any remarkable extent.

Animal 195. Weight 1900 grams. April 4, 1931, 4 cubic centimeters of thorotrast was injected into an ear vein. An X-ray picture taken on April 6 demonstrates the spleen very clearly (Fig. 7). The liver is not clearly demonstrated. The animal died on April 30.

Microscopic examination: The amount of storing cells is still great. However, one sees between the nest of macrophages individual elements which contain either a very small amount of finely granular brown material or none at all, apparently reticulum without phagocytosis (Fig. 8).

Conclusions from the microscopic findings in 4 rabbits injected with thorotrast. At the peak

[1] Radt. Klin. Wchnschr., 1929, viii, 2128.
[2] Radt. Med. Klin., 1930, No. 57.
[3] Oka. Fortschr. Geb. Roentgenstrahlen, vols. xl and xli.

Fig. 1, left. Rabbit 828. Liver and spleen fairly well outlined.
Fig. 2. Same animal, 2 days later.

of the injection there is damage to the overloaded reticulo-endothelial system which seems to become repaired in the later periods.

It may be of interest to point out that two animals (167 and 195) died 18 and 26 days, respectively, after the injection of thorotrast. The amount of thorotrast that these two animals received was reported as a non-toxic dose by Radt. It is possible that the deaths were due to a late harmful effect of thorotrast on liver or spleen or both organs.

Thorotrast has been used in 6 cases on the wards of Mount Sinai Hospital. This group of patients had a large liver or spleen or

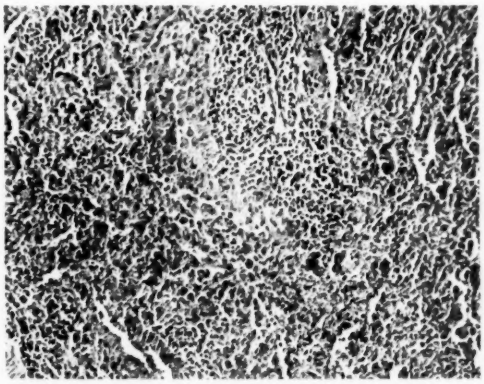

Fig. 3. Low power photomicrograph of section of spleen from same animal as shown in Figure 1.

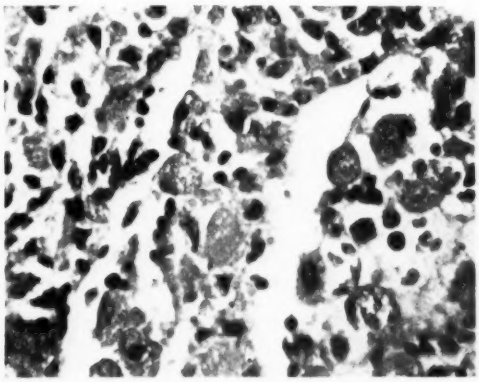

Fig. 4. High power photomicrograph of section of spleen from same animal as shown in Figure 1.

Fig. 5. Rabbit 970. Dim outline of liver.

Fig. 6. Rabbit 167. Liver and spleen clearly outlined.

Fig. 7. Rabbit 195. Spleen clearly outlined.

enlargement of both organs, as demonstrated by palpation. A brief abstract of the histories is given herewith:

CASE 1. 325604. R. W., female, aged 52 years, was admitted May 5, 1931, discharged May 17, 1931. Diagnosis: carcinoma of the stomach with metastasis in the liver. In the right upper quadrant extending almost to the level of the umbilicus there was an irregular and nodular mass which was attached to the umbilicus. A coarser nodular infiltration was present in the ligamentum teres. Test meal showed free hydrochloric acid 0, total acidity 20. X-ray examination of stomach showed a carcinoma. Examination of the abdomen after intravenous injection of thorotrast showed the liver markedly enlarged, reaching down to the iliac crest. The lower half was obscured by intestinal shadows

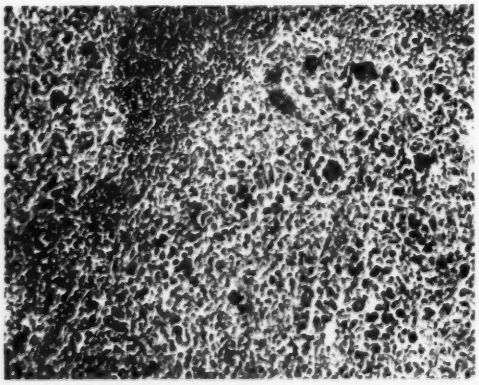

Fig. 8. Low power photomicrograph of section of spleen from same animal as shown in Figure 7.

Fig. 9. R. W. Roentgenogram showing spleen well outlined.

Fig. 10. L. F. Roentgenogram before injection of thorotrast.

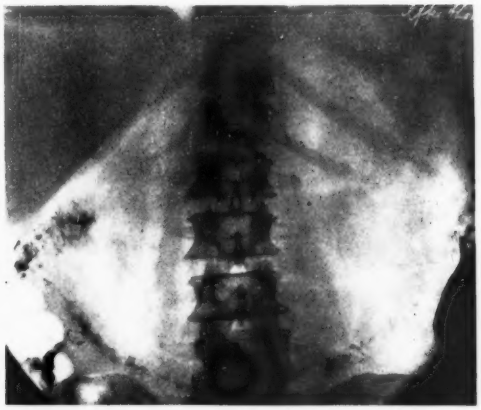

Fig. 11. L. F. Roentgenogram after injection of thorotrast.

so that the possible presence of metastasis could not be determined. Spleen was well outlined (Fig. 9).

CASE 2. 328217. L. F., male, aged 65 years, admitted July 17, 1931, discharged August 13, 1931. Diagnosis: carcinoma of cardia with liver metastasis. Palpation revealed a firm, nodular liver with an irregular edge about 5 fingers below the right costal arch. X-ray examination revealed a carcinoma at the cardiac end of the stomach (Fig. 10). Examination of the abdomen after intravenous injection of thorotrast showed the liver to be somewhat enlarged. No definite abnormalities in the contour were noted. The spleen was not well demonstrated (Fig. 11).

A comparison of Figures 10 and 11 shows that the liver shadow is just as well demonstrated on the flat plate as on the plate taken after the administration of thorotrast.

CASE 3. 324739. S. W., male, aged 40 years, admitted April 8, 1931, discharged May 9, 1931. Diagnosis: inoperable ileocæcal carcinoma with metastasis. Nodular mass in ileocæcal region. The liver was just palpable. The spleen could be felt 2 fingers below the costal margin.

Examination of the abdomen after injection of thorotrast showed the liver and spleen to be fairly well outlined. The spleen was enlarged to a moderate extent (Fig. 12). Exploratory laparotomy (Dr. Aschner) showed an infiltrating lesion of the cæcum with metastasis to the peritoneum and Douglas' pouch.

CASE 4. 329198. R. H., female, aged 55 years, was admitted August 17, 1931, discharged September 20, 1931. Diagnosis: pernicious anæmia. August 18, 7200 cubic centimeters of fluid was removed by paracentesis. A mass was felt in the right abdomen. (Differential diagnosis between kidney and liver.) X-ray examination after thorotrast injection showed

Fig. 12. S. W. Roentgenogram showing liver fairly well outlined.

Fig. 13. R. H. Roentgenogram showing elongated lobe of liver.

Fig. 14. F. A. Roentgenogram showing enlarged liver (carcinoma).

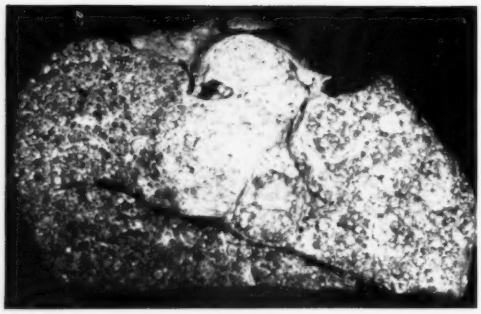

Fig. 15. Same patient as in Figure 14. Postmortem specimen of carcinoma of the liver.

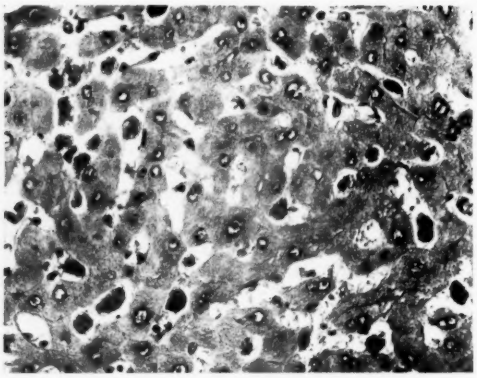

Fig. 16. F. A. Microscopic section of liver, low power.

that this mass was due to an elongated liver reaching down to the crest of the ileum (Fig. 13). Patient improved on liver therapy.

CASE 5. 329380. F. A., male, aged 61 years, was admitted August 24, 1931, died September 16, 1931. Diagnosis: carcinoma of the liver. Jaundice was present for about 1 month. A very large liver was palpable down to 5 fingers below the costal arch. The surface was smooth. X-ray examination after injection of thorotrast showed an enlargement of the liver. The shadow of the liver was dense, but failed to give structural details (Fig. 14). Patient died September 16.

Postmortem examination showed an extensive primary carcinoma of the liver (Fig. 15). Microscopic examination of the liver showed a great number of phagocytes crowded with large granules (thorotrast) within the capillaries of the liver (Figs. 16 and 17).

In the spleen large macrophages with thorotrast granules were found within the reticulum as well as free within the lumen of the sinus.

It is of interest to compare Figures 14 and 15. In spite of the fact that the liver was filled with innumerable large and small carcinomatous nodules, the thorotrast film simply showed the outline of the liver without variation of shadows in the liver substance.

CASE 6. 330104. A. S., male, aged 39 years, was admitted September 14, 1931, discharged October 11, 1931. Diagnosis: cholelithiasis, common duct obstruction (?). Icterus was present for about 4 weeks. The liver was slightly enlarged.

Five doses of thorotrast (12 cubic centimeters each) were given intravenously. Examination of the abdomen after the administration of thorotrast showed the liver and spleen to be distinctly outlined. The liver was moderately enlarged in size, its lower border reaching about 4 centimeters above the crest of the ilium. The spleen was only slightly enlarged. There were no nodules or filling defects noted in either the spleen or the liver (Fig. 18).

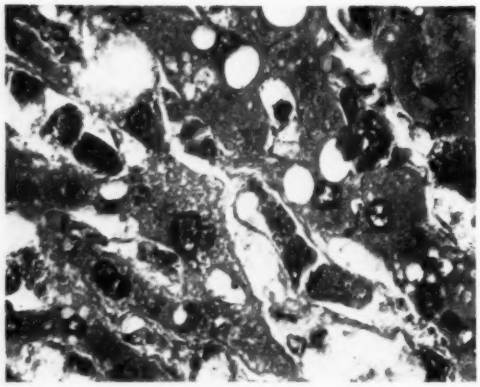

Fig. 17. F. A. Microscopic section of liver under high power.

Fig. 18. A. S. Roentgenogram showing the liver and spleen distinctly outlined.

CONCLUSIONS

1. The intravenous injection of thorotrast in the quantities mentioned has no immediate ill effect on the patient.

2. It is impossible to state at present whether the more or less permanent storage of thorotrast in liver and spleen may not be injurious to the patient.

3. Thorotrast gives an outline of either liver or spleen or both organs without finer details of structural changes in these organs. Its aid in the clinical diagnosis of a pathological condition in the liver and spleen seems to be limited.

4. Thorotrast cannot be compared in diagnostic efficacy with uroselectan and similar drugs in kidney diseases or lipiodol in lung diseases.

I beg to thank Dr. M. L. Sussman, assistant radiologist, for his kind co-operation.

THE RELATION OF PYOGENIC ARTHRITIS TO OSTEOMYELITIS

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PYOGENIC exudative lesions of joints have been classified by Kaufman as primary and secondary arthritides with reference to the avenue of entrance of the infecting micro-organisms. Primary infections may occur as the result of trauma, such as communicating puncture wounds, or a blood borne infection without evidence of a primary focus. Secondary involvement occurs either by metastasis from a remote source with conveyance through the blood stream and occasionally through lymphatic channels (Cotton), or by direct extension from an adjacent pyogenic focus (most frequently osteomyelitis).

That the primary lesions of acute hæmatogenous osteomyelitis are most frequently localized in the diaphyseal extremities of long bones has been well established both clinically and experimentally. Postmortem examinations of patients dying within 48 hours after the onset of symptoms, such as those reported by Starr, repeatedly demonstrated this localization.

Working with rabbits, Bancroft and Robertson obtained similar results and the latter reports the following observations:

"1. Organisms introduced into the blood stream are deposited, among other places, in the long bones.

"2. In bone there is very active phagocytosis except in the metaphysis.

"3. Trauma may determine a local infection.

"4. Growing bones develop abscesses of the type of osteomyelitis within their metaphyses. Adult bones do so rarely. In the presence of a bacteriæmia adults may acquire an arthritis."

In explanation of this phenomenon Lexer outlined the circulatory architecture of long bones by the injection of radio-opaque solutions and he demonstrated at the juxta-epiphyseal region a relatively avascular area where clumps of micro-organisms which were filtered from the blood stream readily establish a focus.

Much has been written relative to primary localization of suppurative processes in the epiphysis, primary suppurative epiphysitis. Uffreduzzi has expressed the opinion that this localization is the rule in infancy, while in childhood the diaphysis is the most frequent site of the original infection. From an extensive experience and careful study, Phemister (7) has concluded that primary suppurative epiphysitis rarely occurs. He has pointed out that if these cases are observed at the onset a primary metaphyseal lesion can almost invariably be demonstrated. In support of this contention and in exemplification of demonstrable direct extension to a joint, Case A is presented.

CASE A. E. S., No. 12716. (Fig. 1.) A girl, 3 weeks of age and with a normal birth, presented no abnormality until the onset of fussiness, swelling, tenderness, and voluntary fixation of the right knee joint during her second week of life. Examination showed a febrile child with no regional changes except for a spindle shaped, tender swelling of the lower end of the thigh and a fluctuant right knee joint with redness of the skin. On admission to the hospital the temperature was 102.8 degrees by rectum and the baby was not acutely ill. The blood Wassermann and Kahn, the tuberculin, and urine tests were reported to be negative. The X-ray examination on admission showed an area of rarefaction (destruction) in the diaphysis of the lower end of the right femur. Subsequent pictures 2 months later demonstrated a progression of the process with destruction of a large portion of the epiphysis. The knee joint was aspirated and a few days later incised and drained; the aspirated pus contained staphylococcus aureus in smear and culture. At 7 weeks of age the right shoulder joint became involved with a repetition of the course followed by the right knee joint.

Since the primary lesion usually finds its origin in the metaphyses, direct extension to, or perforation and drainage into, the adjacent joint occurs in a fair number of cases. After a very comprehensive clinical study of joint complications in hæmatogenous osteomyelitis, Wilensky (14) pictures "fixation points" occurring in the diaphyses with secondary pathological progression to joints. He describes:

(1) extension along lymphatic channels; (2) erosion from "fixation points" in the epiphyses; (3) formation of a sinus leading into a joint by destruction of cortical and cancellous bone; (4) perforation of a subperiosteal abscess into the joint; and (5) simultaneous involvement of both bone and joint by the formation of more than one "fixation point."

Among other factors, such as an advancing thrombophlebitis, this extension to joints is influenced by variance in certain anatomical structures. It is determined to some extent not only by the attachments of the articular capsule, as pointed out by Reich, but also by the reflexions of the synovia, occurring most frequently from bones with complete or partial intracapsular epiphyseal lines. For this reason osteomyelitis of the neck of the femur almost invariably involves the hip joint and frequently infection extends to the knee from the distal extremity of the femur, to the ankle from the lower end of the tibia, and to the elbow from the distal portion of the shaft of the humerus. The importance of the epiphyseal cartilage as a barrier to the spread of bone infection to the adjacent joint is well illustrated by the early and almost universal involvement of joints from bones in which this barrier is lacking. In point, suppurative arthritis is an almost constant complication of osteomyelitis of the small bones of the wrist and ankle. For the same reason such lateral articulations as exist between the upper ends of the radius and ulna and the lower ends of the tibia and fibula (with articular extensions above the level of the corresponding epiphyseal lines) become infected by extension from a process in the end of one of the respective shafts. These facts are well illustrated in the case analyses which are being presented subsequently.

Theoretically, it is possible for a small metaphyseal infection to extend and drain into a joint within a short time after its inception and heal promptly without producing bone destruction or leaving X-ray evidence of the primary focus in the diaphysis. It is conceivable that this may be the explanation of some cases of supposedly primary acute pyogenic arthritis. These cases might be classified as abortive osteomyelitis.

Fig. 1, left. Case A. Note primary localization of infection in the diaphysis of the femur at the onset of osteomyelitis in an infant 4 weeks of age.

Fig. 1A. Case A. The end-result 1 year and 4 months after onset. X-ray evidence of destruction in the medial half of the epiphysis was observed 14 days after the onset.

There is an abundance of indirect evidence that a chronic osteomyelitic process which has originally resulted from an acute hæmatogenous infection may become a focus in itself for the dissemination of bacterial emboli to produce remote bone or joint inflammatory processes. Occasionally, as pointed out by Wilensky (15), an old relatively quiescent lesion has been observed suddenly to show increased activity, as evidenced by a recurrence of pain and an increase in drainage, then a slight rise in temperature and a few hours or days later the appearance of involvement of another bone or remote joint. Presumably a local activation takes place with thrombophlebitis and resultant bacterial metastases. This observation was made in Case 1.

Whether in these cases the infecting microorganisms are ever deposited directly in the synovia of the joint by the blood stream, or are always primarily deposited in the diaphysis from whence they are aborted into the joint, is an interesting speculation. It is most probable that both processes occur. In Beekman's (3) experience, staphylococcus synovial

Fig. 2, left. Case 1. Minimal destructive joint changes with no involvement of adjacent diaphyses; old lesion of the shaft of the fibula. Staphylococcus pus aspirated from this joint.

Fig. 3. Case 2. The joint changes in the right knee are no doubt the result of direct extension from the extensively diseased tibia; those of the left knee joint probably are metastatic.

infections seldom proved to be metastatic. Almost invariably he was able eventually to demonstrate X-ray evidence of a primary lesion in the diaphysis. In accord with this, Wilensky (16) states that a bone lesion is always to be assumed in staphylococcus arthritis but that streptococcus or pneumococcus joint infections are as a rule unassociated with bone lesions.

In a review of 217 cases of acute and chronic osteomyelitis studied at the University of Chicago Clinics over a period of 4½ years, 9 cases presented evidence in their histories and physical and late X-ray examinations of pyogenic arthritis without evidence of osteomyelitis in the adjacent diaphyses, that is, 4.1 per cent. Of the 9 cases, 4 presented joint involvements which may have had their inception with the original blood stream invasion and accompanying showers of bacterial emboli; and 5 developed late in the course of the disease presumably from secondary metastases from osteomyelitic foci. The joints involved were the temporomandibular in 3 cases, the hip, knee, and elbow, each in 2 cases. These reports, based upon observations made during the end-result stage of pyogenic arthritis, afford no statistical bacteriological data, but staphylococci were cultured from other foci in bone in 7 of the 9 cases.

Forty-two cases (19.3 per cent) presented evidence of pyogenic arthritis by direct extension with involvement of 53 joints. Extension occurred from the femur in 23 cases, the tibia in 16, the ilium in 8, the humerus in 3, the tarsal bones in 2, and the carpal bones in 1 case. The joints involved with respect to the bones from which extension occurred are as follows:

	Instances
Knee (19 cases, 36 per cent):	
Distal end of femur	13
Proximal tibia	6
Hip (14 cases, 26.4 per cent):	
Proximal femur	10
Ilium	4
Ankle (12 cases, 22.6 per cent):	
Distal tibia	10
Tarsal bones	2
Sacro-iliac (4 cases, 7.5 per cent)—ilium	4
Shoulder (2 cases, 3.8 per cent)—humerus	2
Elbow (1 case, 1.9 per cent)—humerus	1
Wrist (1 case, 1.9 per cent)—carpal bones	1

(Of the entire series of 217 cases of osteomyelitis, the tarsal bones were involved in two instances, the carpals in only one. However, in all three cases the infection extended to the adjacent joints.)

Three cases presented joints involved both by direct extension and metastasis. In 9 cases of the entire series there was record or a

definite history of the institution of surgical drainage of the joints. Three were drained by repeated aspirations with return of a complete range of motion, and, of the 6 treated by open drainage, 3 subsequently became ankylosed, 1 developed a full range of motion, and 2 regained about 50 per cent of normal function.

A comparison of the end-results in these two groups of cases tabulated later indicates that ankylosis results more frequently in the joints involved by direct extension than those involved presumably by metastasis.

	Infection by			
	Direct extension		Metastasis	
	Cases	Per cent	Cases	Per cent
Ankylosis	34	65.2	4	44.5
Limited motion	12	22.6	2	22.2
Full range motion	7	13.2	3	33.3
Total joints	53		9	

CASE REPORTS

(Illustrative of metastatic hæmatogenous pyogenic arthritis)

CASE 1. R. W., male, aged 7 years (Fig. 2), admitted in September, 1929, with a history of good health until the onset of the present illness in April, 1929. Three days following injury, the right heel became severely painful and the boy became delirious, with a temperature of 106 degrees F. Two days later an abscess appeared on the medial side of the right heel, and the patient was taken to a hospital where drainage was established. In the course of the following month, abscesses appeared in the left arm and the left leg. The patient was then taken home, but returned to a hospital 3 months later with swelling and pain in the left knee joint. This was aspirated and irrigated, with a prompt recovery. A transcript of the hospital record showed that the aspirated pus contained staphylococcus aureus in smear and culture.

April 25, 1931, the patient complained of pain in the right heel and the discharge from the sinus greatly increased and was slightly blood tinged. Three days later the left knee swelled and became somewhat painful. The swelling promptly subsided with very little further impairment of function. Examination at the present time shows a discharging sinus on the medial aspect of the right heel, scars on the lateral side of the lower third of the left humerus and the middle half of the outer surface of the left leg. There is slight limitation of motion in both the right elbow and left knee joints. Wassermann and Kahn examinations of both patient's and mother's blood were negative. Tuberculin (1:100) was negative. The X-ray films showed osteomyelitis of the right os calcis and the mid-shaft of the left fibula, and a destructive arthritis of the left knee joint.

CASE 2. E. K., male, 4 years of age (Fig. 3). The patient was perfectly well until 2 years of age, when he was picked up from the sidewalk apparently delirious, with a fever and pain. Two days later the left leg swelled and the patient was taken to a hospital. The subsequent history was compatible with acute osteomyelitis involving several bones. Examination at the present time shows multiple scars of old sinuses over the left clavicle, right lumbar region, left fibula, right tibia, and distal right humerus. The right leg is 1½ inches longer than the left, and there is some limitation of motion in both knee joints. The Wassermann, Kahn, and tuberculin tests were negative. The radiograms showed areas of osteosclerosis of the left clavicle, both iliac alæ, distal shaft of the right humerus, upper three-fourths of the right tibia, and middle third of the left fibula, and a destructive arthritis of both knee joints.

Fig. 4. Case 3. Note destructive arthritis of the left hip joint with erosion at the points of greatest contact and pressure; also pathological dislocation of the right femur and osteomyelitis of the wing of the right ileum.

This case demonstrates multiple but presumably healed foci of osteomyelitis with involvement of two joints. The right knee displays extension from the adjacent diaphysis of the tibia, while the arthritic changes in the left knee joint appear to be the result of a hæmatogenous infection, for there is no evidence of a pre-existing osteomyelitis in the adjacent tibial and femoral diaphyses.

CASE 3. F. S., No. 22095, male, aged 11 years (Fig. 4), admitted to the hospital April 24, 1930, gave a history of very good health until the onset of the present illness in August, 1929. On the day

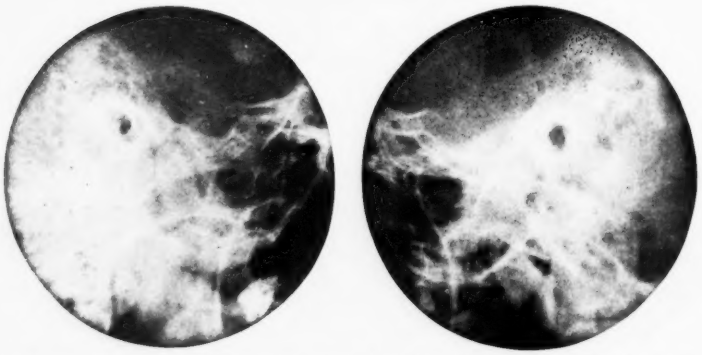

Fig. 5. Case 4. (Illustrative of Cases 5 and 6.) Note obliteration of the joint space of the right temporomandibular joint. Its outlines can scarcely be made out.

following an injury received while swimming he suddenly developed a chill, severe pain in the right hand and left leg and foot. Swelling and redness of the leg rapidly followed, and 10 days later both hips became painful. Three months after the onset, spontaneous drainage of thick, yellow pus occurred over the left great toe, and a few weeks later the same occurred in the left leg. There was a history of frequent attacks of tonsillitis. On April 26, 1930, partial ostectomies of the lower third of the left tibia and interphalangeal joint of the left great toe were done. The pathological report was pyogenic osteomyelitis and the cultures yielded staphylococcus aureus. The Wassermann, Kahn, tuberculin, and urine tests were negative.

The present physical examination shows a discharging sinus of the medial aspect of the lower third of the left leg, and scars on the dorsum of the great toe and lower third of the right humerus. The left ankle is ankylosed with 15 degrees' plantar flexion, the right leg in 45 degrees' abduction and 50 degrees' external rotation. The X-ray films show osteomyelitis of the ala of the right ilium and the lower third of the left tibia, with bony ankylosis of the adjacent tibio-astragaloid joint, and osteoarthritis of the left knee, left shoulder, and both hip joints. The head of the right femur is dislocated upward with erosion of the acetabulum and femoral head.

Of special interest in this case are the X-ray evidences of bone destruction of the femoral head and the rim of the acetabulum at the points of greatest contact and pressure in the joint (Phemister, 16).

Case 4. R. J., No. 26877 (Fig. 5), a white male aged 18 years, admitted August 10, 1930, gave a history of an injury over the right tibia 3½ years before admission, followed by a painful swelling and 2 months later spontaneous drainage. Then swelling and likewise spontaneous drainage occurred at the left elbow, left middle finger, and over the left scapula. All foci promptly healed with the exception of that in the tibia. He had pain in the right temporomandibular joint during the acute illness and about 6 months later noticed a gradual progressive blocking of his jaw, with pain and swelling.

The physical examination was negative except for scars over the sites noted and a spindle shaped enlargement of the right tibia with a long suppurating sinus and ankylosis of the right temporomandibular joint. The routine laboratory studies of the urine and blood, the Wassermann, Kahn, and tuberculin tests were negative. The X-ray examination showed evidence of an old sclerosing osteomyelitis of the upper half of the right tibia, osteomyelitis with cavitation of the mid-shaft of the left humerus, and an ankylosing arthritis of the right temporomandibular joint with obliteration of the joint space.

August 26, 1930, an arthroplasty was done on the right temporomandibular joint. Bone removed at subsequent operations on the right tibia and left humerus was reported to present the pathology of osteomyelitis, and staphylococcus aureus was shown in smear and culture. Eleven months after the arthroplasty the mouth could be opened normally.

Case 5. C. B., No. 61, a white male of 21 years, admitted October 5, 1927, gave a history of onset of osteomyelitis 6 years previously, with delirium, and involvement of the left femur, right tibia, left scapula, left and right metatarsus, left tibia, right ischium, right fibula, right ulna, and right humerus, in rapid succession. These foci were all drained and the staphylococcus aureus hæmolyticus was cultured from them. Soon afterward pain and swelling developed in front of both ears and both jaws gradually became ankylosed. Arthroplasties were done on both joints. During the first 3 years of this illness the boy had repeated small hæmoptyses, and a diagnosis of pulmonary tuberculosis was made and verified by the presence of tubercle bacilli in the sputum. The blood Wassermann, Kahn, and urine tests were negative.

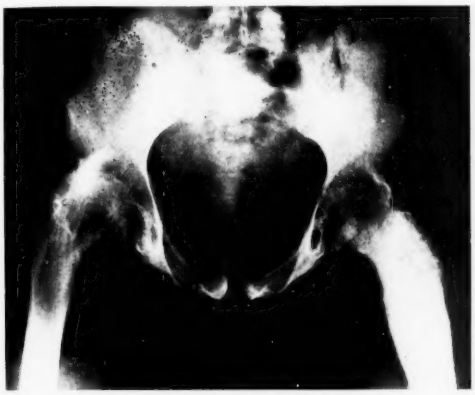

Fig. 6. Case 8. Ankylosis of right hip joint with no involvement of adjacent bone. The left hip obviously infected by extension from the head, neck, and shaft of the left femur.

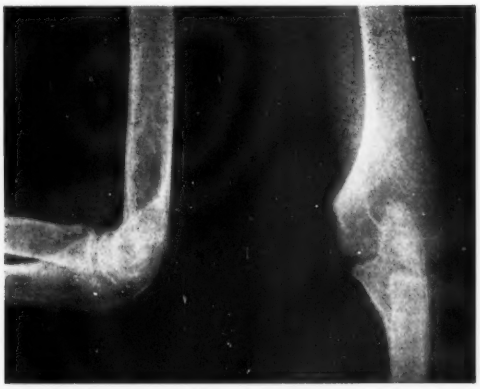

Fig. 7. Case 9. There is a definite arthritis with some limitation of motion; a bulbous enlargement of the proximal extremity of the ulna.

The patient was admitted to the hospital at this observation for a secondary arthroplasty of the left temporomandibular joint. The result was very satisfactory.

Case 6. L. B., No. 17938, a white woman 33 years of age, admitted December 13, 1929, gave a history of osteomyelitis of the left tibia of 13 years' duration, coming on with a stormy onset 2 days after a puncture wound of the left great toe. Early drainage had been established and two subsequent operations upon the left tibia had been performed. For 6 months the patient had had pain in the left temporomandibular region, and difficulty in opening her mouth.

Examination revealed healed scars over the medial and lateral aspects of the lower two-thirds of the left tibia, considerable limitation of motion in the left knee, and ankylosis in the left ankle joint. Some limitation of motion and marked tenderness of the left temporomandibular joint were noted. The X-ray studies indicated an osteomyelitis of most of the shaft of the left tibia with a sequestrum and fusion to the fibula, ankylosis of the left ankle joint, and changes in the left femoral condyle, with no definite bone changes in the left temporomandibular joint. The Wassermann, Kahn, urine, and blood studies were negative.

Sequestrectomies of the left tibia were done December 21, 1929, and November 26, 1930. Staphylococcus aureus was found in smear and culture.

Cases 4, 5, and 6 present an added interest as a series of ankylosing arthritis of the temporomandibular joint. All subsided without drainage.

Case 7. R. C., No. 1553 (Fig. 5), a white boy of 5½ years, entered the hospital January 4, 1928, with a history of osteomyelitis of 2½ years' duration, involving the left femur, the left tibia and ankle, the left humerus, the left ilium, and the right side of the skull.

Examination showed healed scars over the left elbow joint, the right lateral occipital region, the left lower leg and ankle, and a discharging sinus over the left hip. Roentgenograms revealed multiple healed or healing osteomyelitic foci of the skeleton, with an active process in the right humerus and an arthritis of the left elbow. The blood Wassermann, Kahn, urine, and tuberculin tests were negative.

Partial ostectomies were done on the right humerus and left ilium December 2, 1928. Staphylococcus aureus was found in smear and culture, and bone sections were reported to be osteomyelitic.

Case 8. R. M. H., No. 25661 (Fig. 6), a girl of 10 years, admitted to the hospital August 25, 1930, reported good health until she suffered a puncture wound, 6 months before admission, in the right thigh, followed a few days later with a cellulitis and lymphangitis. This promptly healed and 2 weeks later she developed clinical evidence of a bacteriæmia, but had negative blood cultures. In the course of the next few weeks there developed a pleurisy, superficial abscesses, and osteomyelitic foci in the right first metatarsus, the upper one-third of the right tibia, the lower one-third of the right radius, the upper one-third of the right humerus, and the upper thirds of the left humerus and left tibia. All foci were drained apparently by simple incision of the overlying soft tissues. Five months after the onset of the present illness and 2 weeks before admission, the right hip became painful and tender for the first time and was associated with fever and ill feeling.

The examination revealed a granulating sinus at the base of the right great toe, and tender enlarge-

ments over the upper ends of both tibiæ and both humeri, and the lower one-third of the right radius. The right hip was fixed in flexion with limitation of, and pain in, all motions; there was also tenderness over the greater trochanter. The laboratory studies, including blood Wassermann, urine, blood, and tuberculin, were negative except for evidence of a moderate anæmia. Roentgenology demonstrated osteomyelitis of both humeri, both tibiæ, first right metatarsus, and the right radius, and a pyogenic arthritis of the right hip joint.

Partial ostectomies were done on both tibiæ, both humeri, the right radius, and the right first metatarsus. Microscopic sections revealed chronic osteomyelitis. The right hip was never drained and subsided with ankylosis.

CASE 9. L. H., No. 7964 (Fig. 7), a white male aged 14 years, entered the hospital November 13, 1928, with a history of osteomyelitis of the left femur, right fibula, and sacrum of 3½ years' duration, apparently not coming on abruptly.

Examination showed marked cardiac hypertrophy with decompensation, marked enlargement of the liver and spleen, and draining sinuses over the right fibula and left hip. The left elbow and left shoulder were greatly limited in motion. The roentgenograms showed arthritic changes in the left elbow, osteomyelitis of the proximal end of the left humerus with involvement of the shoulder joint, the wing of the left ilium, the left femur, with destruction of the entire head and neck, and the right fibula with absence of most of its shaft. The urine consistently contained a large quantity of albumin with an occasional granular cast. The hæmoglobin was 65 per cent, the red blood count 4,800,000, the blood Wassermann and Kahn negative. 100 per cent of Congo red, injected intravenously, was absorbed.

The patient was discharged with a diagnosis of chronic suppurative osteomyelitis with multiple foci, and amyloid degeneration of the liver and spleen.

SUMMARY

1. Of 217 cases of pyogenic osteomyelitis there was associated arthritis in 51 cases, an incidence of 23.5 per cent.

2. Of these 51 cases, 42 (19.3 per cent) arose by direct extension from an adjacent diaphyseal infection. The large weight bearing joints constituted 92.5 per cent of this group.

3. In 9 cases (4.1 per cent) the joints appeared to have become involved by blood borne infections, presumably from remote foci of osteomyelitis. However, there may have existed at some time a small undiscovered lesion in the adjacent bone, and the joints may represent the end-result of an abortive osteomyelitis.

4. The seriousness of this complication of osteomyelitis has been measured in this analysis by the end-results of the joint damage alone. Only 13.2 per cent of joints infected by direct extension regained a good range of motion, 65.2 per cent became ankylosed, and the remaining 22.6 per cent suffered varying degrees of functional limitation.

A comparison of these end-results with those resulting from hæmatogenous infection, in the small series analyzed, suggests that less joint damage is produced by the latter type. In this group ankylosis occurred in 44.5 per cent and a good range of motion was preserved in 33.3 per cent of the cases.

BIBLIOGRAPHY

1. BANCROFT, F. W. Acute hematogenous osteomyelitis. Ann. Surg., 1921, lxxiii, 681.
2. BEEKMAN, F. Acute hematogenous osteomyelitis. Ann. Surg., 1928, lxxxviii, 270–296.
3. Idem. Acute hematogenous osteomyelitis. Bull. N. Y. Acad. Med., 1930, December, 6–792.
4. COTTON, F. J. Infections of bones and joints. Surg., Gynec. & Obst., 1925, xl, 658.
5. KAUFMAN, EDWARD. Lehrbuch der Speciellen Pathologischen Anatomie. Berlin: Reimer, 1922.
6. LEXER, E. General Surgery. Bevan, A. D. New York: Appleton & Co., 243, 1908.
7. PHEMISTER, D. B. The pathology and treatment of pyogenic arthritis. Pennsylvania M. J., 1928, xxxii, 52–57.
8. Idem. Effect of pressure on articular surfaces. Ann. Surg., 1924, lxxx, 481.
9. REICH, R. S. Purulent arthritis. J. Bone & Joint Surg., 1928, x, 554–578.
10. ROBERTSON, D. E. Acute hematogenous osteomyelitis. J. Bone & Joint Surg., 1927, ix, 8–23.
11. STARR, C. L. Acute hematogenous osteomyelitis. Arch. Surg., 1922, iv, 567–587.
12. Idem. Dean Lewis' Practice of Surgery. Vol. ii, Chapter 2, 6–8.
13. UFFREDUZZI, O. Latent microbism of the epiphysis. Arch. ital. de chir., 1925, xii, 300–348.
14. WILENSKY, A. O. Joint complications of acute osteomyelitis or acute epiphysitis. Ann. Surg., 1927, lxxxvi, 737.
15. Idem. Arch. Surg., 1926, xiii, 895.
16. Idem. Pathogenesis of end results of lesions of acute osteomyelitis. Ann. Surg., 1926, lxxxiv, 651–662.

CLINICAL SURGERY

FROM ST. LUKE'S HOSPITAL, KANSAS CITY

THE SHELF OPERATION IN THE TREATMENT OF CONGENITAL DISLOCATION OF THE HIP

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GENERALLY speaking, in the treatment of congenital dislocation of the hip, two methods are employed; reduction by closed manipulation, reduction by operation. Actually, however, there is a third method of treatment which must be used at times which cannot be included under the term "reduction" since it does not attempt replacement of the dislocation but has for its object the relief of symptoms and improvement in function in a dislocated hip which cannot be reduced. Reduction by manipulation is, at the present time, fairly well standardized; at least it may be said that the basic principles of the manipulative method have been established and most of the methods in common use conform to these principles. The technique of reduction by operation was established by Galloway, in 1920, and this technique, with such modifications as the individual operator may have chosen to make, is generally used today. For the treatment of congenital dislocation of the hip in those cases in which it is impossible actually to reduce the dislocation, a variety of procedures have been devised. One of these procedures, the shelf operation, it is proposed to discuss in this contribution.

In the management of congenital dislocation of the hip the factor which most profoundly influences the course to be followed is the age of the affected individual. Age is of paramount importance because it not only determines when closed reduction should be abandoned and reduction by operation resorted to, but also what type of operative procedure is to be employed. It is, then, impossible intelligently to discuss any form of treatment for congenital dislocation of the hip without taking into consideration the age factor, and a brief discussion of the way in which age influences the selection of the method of treatment used becomes a necessary preliminary to a discussion of a specific form of treatment such as the shelf operation.

For the purpose of this discussion we will separate cases of congenital dislocation of the hip into three age groups. These groups represent approximately the important age periods in so far as treatment is involved. These groups are:

Group I. Patients up to 4 years of age.

Group II. Patients from 4 to 9 years of age.

Group III. Patients over 9 years of age.

In using the age periods shown in these three groups we recognize that no sharp lines of demarcation can be drawn; they are meant to be an approximate guide, not an absolute one. Our experience, however, leads us to believe that these groups truly represent definite dividing lines in the treatment of congenital dislocation of the hip.

Group I. This group may be briefly dismissed with the statement that practically every congenital dislocation of the hip in patients up to the age of 4 years can be successfully reduced by one of the methods of closed manipulation in use. Occasionally, however, closed reduction within this age limit is impossible and reduction by the open method must be resorted to. In our clinic open reduction in patients under the age of 4 years has been necessary in only 2 cases in 10 years.

Group II. In Group II we enter upon debatable ground. Many experienced orthopedic surgeons hold that the closed method of reduction should be used in children up to the age of 7 years and even up to 10 years. Others are convinced that closed reduction should be abandoned when a child has reached the age of 4 years and the open method of reduction used. Galloway, with a wide and successful experience, advocates reduction by operation at 2½ years and considers 20 months to be the ideal age for this method. Experience over the past 12 years, during which time 71 congenital dislocations of the hip have been treated, has convinced us that, in our hands at least, the best results are secured by reducing all dislocated hips over the age of 4 years by the open method.

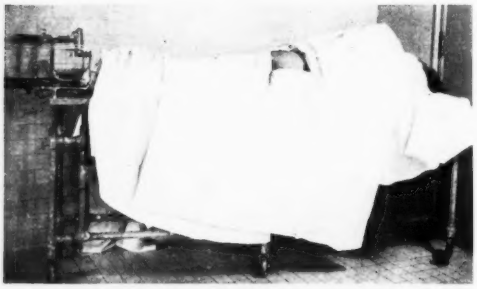

Fig. 1. Position on operating table; patient turned slightly toward non-operative side.

Fig. 2. The Smith-Petersen incision.

However, whether reduction by operation is used in patients at the age of 4 years, or earlier, or later, it is possible, by the open method, in the majority of patients up to the age of 9 years to return the head of the femur to the acetabulum, and the result should be a physiological cure. As stated previously the technique of Galloway is entirely satisfactory for open reduction in this age group.

Group III. After the age of 9 to 12 years, we believe 9, the picture of congenital dislocation of the hip changes rather suddenly. Up to this age, as has been pointed out, the dislocated femoral head can in the majority of cases be restored to the acetabulum by either the closed or open method; in children over 9 years of age such reduction is generally impossible or if possible, undesirable. Reduction is impossible because the thickened and contracted capsule and the extreme shortening of the muscles which pass from the pelvis across the hip joint to the femur prevent, except by using extreme force and running unjustifiable risks, the displacement of the head downward sufficiently to allow it to enter the acetabulum. Reduction is undesirable in these cases because, even if the reduction can be accomplished by the use of great force, the head is thrust so strongly against the acetabulum by the contracted structures about the hip joint that absorption of the articular cartilage follows and rigidity or complete ankylosis will result in a very high percentage of the cases. Ankylosis, or even marked limitation of motion, is a very disabling condition and the strong probability that it will occur constitutes a definite contra-indication to replacing the femoral head in the acetabulum in these older cases. Our problem in Group III then is quite different than in Groups I and II, and our treatment must in the majority of cases aim at stabilizing the hip and improving the function of the joint without restitution of the dislocated head. We must, in other words, abandon the ideal of a physiological cure, possible in Groups I and II, and be satisfied with what Kreuz, of Berlin, has termed a pathophysiological cure.

Efforts to devise a satisfactory method of stabilizing a congenitally dislocated hip and at the same time preserve a useful amount of motion without restoring the dislocated head to the acetabulum have produced a variety of operative procedures. These include the methods of Allison and Swett which attempt to restore the head to the acetabulum, even in older patients, by a two stage operation; the Lorenz, von Baeyer, and Kurmisson bifurcation operations; the Shanz osteotomy; and the shelf operation. The last of these, the shelf operation, has been used routinely in our clinic for the past 12 years, and it is the technique of this operation we propose to discuss in detail.

The shelf operation for congenital dislocation of the hip aims: (1) to improve the weight bearing position of the head of the femur by bringing it forward from its position on the posterior plane of the pelvis to a position on the ridge between the anterior and posterior planes or onto the anterior plane itself, thus overcoming lordosis; (2) to stabilize the dislocated hip for weight bearing purposes; (3) to preserve a useful amount of pain free motion in the hip. To accomplish these three cardinal purposes we believe that a definite technique is necessary; the procedure as carried out in our clinic has varied but little from that

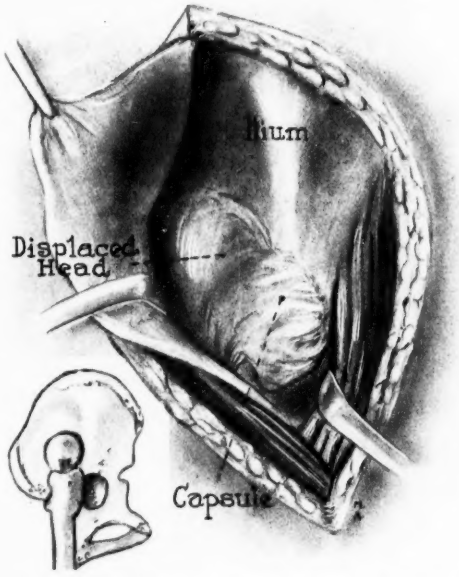

Fig. 3. The incision has been deepened to expose the capsule and displaced head lying in the posterior plane of the pelvis above and posterior to the true acetabulum.

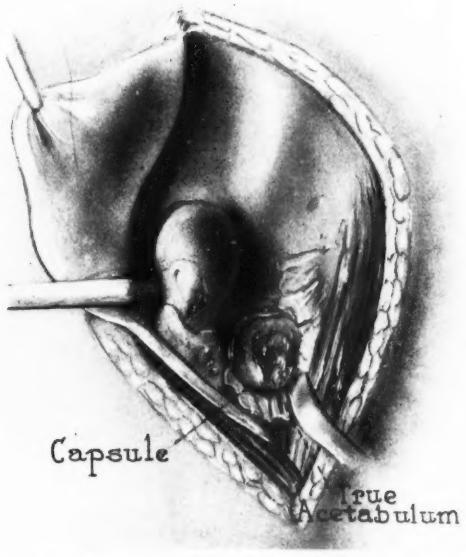

Fig. 4. The capsule has been cut away and all restricting structures divided or stripped back, and the head is completely free. The lever is in position to slide the head forward onto the ridge between the anterior and posterior planes of the pelvis or onto the anterior plane.

described by the author in the *Journal of Bone and Joint Surgery* of 1924, and is as follows:

TECHNIQUE

Preliminary preparations. Skeletal traction is applied for 2 weeks by means of a Kirchener wire passed through the crest of the tibia just below the tuberosity. Notwithstanding the assertion frequently made that little relaxation of contracted structures may be expected from traction preliminary to operation for congenital dislocation of the hip, experience has convinced us that when skeletal traction is used a definite amount of relaxation is secured and that the dislocated head can be much more easily displaced at operation than in these cases in which such preliminary traction is not used. From 10 to 15 pounds of weight are used, depending upon the age and physical condition of the patient.

Operative preparation. The operative field prepared extends from the umbilicus to the knee on the side to be operated upon and includes half of the pelvis and the entire thigh. A double preparation is given, one at noon of the day before the operation and the second in the late afternoon. On the operating table the entire area is painted with a 2 per cent iodine solution. The pubic hair, if present, is shaved.

Placement on the operating table (*Fig. 1*). Some form of traction operating table must be used. The patient is placed upon the table with traction applied to both legs; the traction already in place (Kirchener wire) is used on the side to be operated upon and skin traction is used on the opposite leg to secure countertraction and to anchor the pelvis. Only sufficient traction is applied to hold the patient on the pelvic support; this allows the patient to be rolled slightly toward the side not to be operated upon and affords better access to the region to be operated upon.

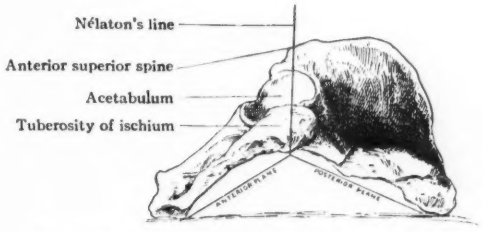

Fig. 5. The anterior and posterior planes of the pelvis are shown with ridge between. (From Davis' *Applied Anatomy.*)

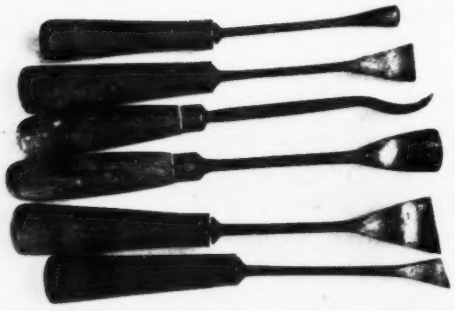

Fig. 6. Woodcutter's gouges of various sizes.

The steps of the operation are as follows:

1. The Smith-Petersen incision, which runs from well back on the iliac crest down onto the thigh, is used (Fig. 2). This incision is the only one which gives sufficient exposure to allow the subsequent steps of the operation to be carried out efficiently. The skin edges are protected by towels fastened with tetra clamps. The incision is deepened in the usual manner until the capsule of the joint is reached and freely exposed (Fig. 3).

2. The dislocated head is now completely freed of all structures which interfere with complete mobility. This is accomplished by freely and completely cutting away all the thickened capsule and by dividing all fibrous bands. Muscle attachments which interfere, particularly those to the greater trochanter, are preserved as far as possible by stripping up their periosteal attachments. Generally, it is necessary to divide the tendon of the iliopsoas which is usually markedly shortened; no ill effects have followed this. The importance of completely freeing the upper end of the femur cannot be overemphasized; attempts to preserve the capsule prevent this and are unnecessary as it regenerates later (Fig. 4).

3. The head, neck, and upper part of the greater trochanter having been completely freed, traction on both legs is gradually increased. As the traction force acts, the elevated side of the pelvis is allowed gradually to sink until the patient is lying flat on the table. At this point a lever (Fig. 4) is placed behind the head and neck and, if the upper end of the femur has been adequately freed, the head readily slips forward onto the ridge between the posterior and anterior planes of the pelvis (Fig. 5) into a position above, or above and slightly in front of, the acetabulum. Traction is then gradually increased until the head has been pulled down in its anterior position

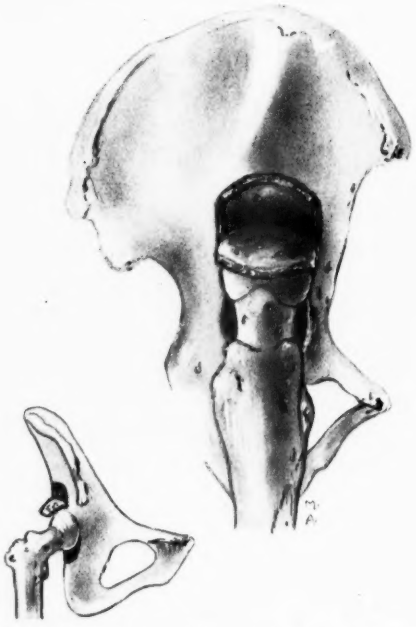

Fig. 7. Flap is turned down coming well down both anteriorly and posteriorly and covering the femoral head like a cap.

to a point beyond which it will not descend without the use of unjustifiable force; this is as a rule about an inch to an inch and a half. Both lower extremities are then gradually abducted and the traction is tightened to take up the slack which usually follows this maneuver. The head is now in the position in which, by turning down a flap or shelf of bone from the side of the ilium, it is to be held permanently.

4. The shelf is formed as follows: A woodcutter's gouge (Fig. 6), the size depending upon the size of the shelf to be formed, is used to turn down a flap of bone from the side of the ilium. This flap should be 1.5 to 2 inches in depth and at least 0.5 inch thick at its base. The flap should start well anterior to the head and be continued over it and well down posteriorly, so that when the shelf is completed it fits over the upper part of the head like a cap (Fig. 7). It should be understood that the shelf turned down is not merely a ledge of bone projecting from the ilium but a modelled covering for the femoral head. A large wedge of bone is then removed from the crest of the ilium, or several wedges if so desired and this is securely fixed between the turned

Fig. 8. Wedge of bone has been removed from the crest of the ilium and fixed between the side of the ilium and the turned down flap.

down shelf of bone and the side of the ilium, filling the space between them (Fig. 8). The wedge of bone acts as a brace for the turned down flap and provides a firm shelf above the head capable of resisting a fairly strong upward thrust without giving way.

5. At this point the condition of the adductor tendons of the thigh is examined; if they are under tension, an assistant does an open tenotomy of these tendons before closure of the wound is commenced.

6. Closure of the wound is made in the usual manner by layers. Drainage is rarely used and, if used, consists of a piece of rubber dam placed just under the skin and removed in 12 hours.

7. A plaster-of-Paris cast is now applied to include both hips and to extend down to just below the knee on the side which has been operated upon. The patient is transferred directly to bed from the operating table, strong traction on the extremity operated upon being maintained constantly by an assistant during this transfer and until the traction apparatus attached to the bed has been arranged and is acting.

Fig. 9. Roentgenogram showing type of shelf secured.

After-treatment. Traction is maintained constantly for 6 weeks. At the end of the fourth week, the cast is bivalved and mild flexion and rotation movements are given daily. After 6 weeks traction is discontinued and physiotherapy continued with gradually increasing range of motion insisted upon. Weight bearing is started at the end of 6 weeks with crutches and at the end of 8 weeks unrestricted weight bearing is permitted. It is necessary to maintain supervised exercises for several months following operation in order to secure full range of motion.

RESULTS

The results to be expected from a properly performed shelf operation are:

1. A stable, pain free, freely movable hip, with limitation of motion only in the extremes of the arc.

2. Improved weight bearing with improvement or disappearance of lordosis and its accompanying symptoms of backache.

3. A definite decrease in the shortening which, on the average, is about 1 inch.

4. Improved walking because of the resulting stability and lessening of the give in the hip on weight bearing.

We have performed the shelf operation in 26 dislocated hips with the following results:

	Cases	Per cent
Good results	21	80.7
Improved	2	7.6
Failures	3	11.5

The youngest patient operated on was 9 years old; the oldest, 40 years old.

The failures were due in one case to a low-grade infection which resulted in ankylosis but with improvement in position. The second failure was not one of failure to secure stability and motion but, since the operation, the patient has suffered from very marked symptoms in the sacro-iliac joint on the side operated upon. The third failure was due to an attempt to secure too much length with resulting pressure on the head with absorption of articular cartilage and rigidity in the hip.

There have been no deaths in the 26 cases operated upon nor have any serious complications occurred. Unduly prolonging the operation and attempting to obtain too much lengthening should be avoided, as they tend to cause shock.

The results of the shelf operation, so far as we can determine, have been lasting. Four patients were operated upon 12 years ago and all are leading active lives without symptoms or any interference with active use of the hip. The same results are being obtained in more recent cases, as shown in Figure 9.

CONCLUSIONS

In conclusion, may I say that it is my firm belief that before many years have passed the question as to what is the best operative procedure for neglected cases of congenital dislocation of the hip will rarely come up for decision because, as the public and profession become educated, practically all cases will fall in Groups I or II when physiological cure is possible. It is in the first 3 years of life that congenital dislocation of the hip must be treated if it is to be cured completely so that the most important step in the management of congenital dislocation of the hip, as I see it, is the untiring preaching of the gospel of early diagnosis and early correction. The various operations for treatment of the long standing, or perhaps better, the neglected cases, are makeshift procedures which, it is true, fulfill a definite purpose but they, by their very existence, constitute a reproach to the medical profession.

FROM THE SURGICAL CLINIC, UNIVERSITY OF FRANKFURT A. MAIN

WIRE EXTENSION TREATMENT OF FRACTURES OF FINGERS AND METACARPAL BONES

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THERE are three points of importance to be kept in mind in treating fractures of the fingers and metacarpal bones: (1) The ends of the fragments must be brought into a position which is absolutely faultless anatomically. (2) Fractures of the fingers and metacarpals are especially apt to result in great dislocations and for this reason the correct position of the fragments should be judiciously maintained until the formation of callus prevents the fragments from being dislocated and shoved against one another. (3) Physical therapy must be begun as early as possible, lest the wrist and the joints of the fingers grow stiff. Usually it is not so difficult to obtain an exact reposition of the fragments as it is to keep them in position and, without again dislocating the fragments, to start exercises early. The contraction produced by the tendons and aponeuroses works to a disadvantage upon the maintenance of the fixation of the fracture, and may prove to be a real danger when physical therapy, which is absolutely necessary, is begun early. We know that fingers and wrists, especially, grow stiff very quickly when they are held in a fixed position. It is always a question whether the patient will be able to make use of his hand in a normal way after it has been kept at rest for some time or whether he will be incapacitated economically as well as psychologically. In a study by Ziegler of a series of 403 cases of fractures of the fingers, the percentage of invalidism was found to be an average of 24.9 per cent.

The two problems, the maintenance of fixation and early orthopedic treatment, have brought forth many therapeutic proposals. In a recent, more detailed contribution[1] I suggested that the methods hitherto proposed had certain disadvantages which led to disappointing results. The various types of splints for the hand and the fingers do not prevent new dislocations of fragments after they have been well and properly aligned. The method of fixing the hand with fingers closed over a roll of gauze has the same disadvantages; moreover, the fingers which are not involved are fixed as well. The method of extending the parts by means of adhesive plaster is not only very disagreeable to the patient but the wrist and the joints of the fingers are stretched in a way not physiological, and the result is again disappointing. This method, too, has still another disadvantage in that in certain cases sufficient pressure cannot be procured from the adhesive plaster without exposing the tip of the finger to the danger of being insufficiently nourished. Without entering into particulars I would refer to my contribution just mentioned.

I have tried to overcome all of the disadvantages referred to by making an apparatus for extension of the finger by means of wire. The chief points of interest are as follows:

1. The apparatus should make it possible to exert traction strong or mild according to the conditions met in a given case.

2. The finger which is to be extended and the wrist which is to be fixed should be brought into a physiological position which is agreeable to the patient and which will facilitate and shorten the period of treatment to restore function.

3. It is absolutely necessary that while fixed and extended by means of the apparatus the finger affected as well as the other fingers can be exercised in order to provide against the danger of stiffness.

4. It is essential that the apparatus be so constructed that it can be used to extend each finger and to take the place of the cuff of plaster of Paris used on the forearm, the application of which requires much time.

On the basis of these postulates and after having been tried thoroughly, the apparatus is now made (by Braun-Melsungen) as shown in Figures 1 to 5.[2] It may be described briefly as follows:

There is a forearm cuff made of neat leather which is adjustable to different size wrists. By three straps a narrow Kramer splint is fixed in such a manner that its form and direction may be altered according to the kind and the situation of the fracture. By means of a spiral spring at

[1] Chir., 1932, p. 58.

[2] The apparatus can be obtained from the American Medical Specialties Co. Inc., 352 Seventh Avenue, New York.

Fig. 1. Finger extension and bow to produce traction.

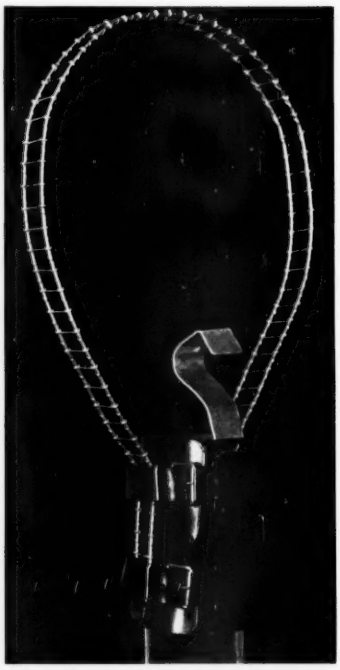

Fig. 2. Forearm cuff of leather with Kramer splint and aluminum prop which is bent to fit the hollow of the hand.

the end of the Kramer splint, there is applied for extension a light and narrow bow holding a thin steel wire which is rust proof, according to Kirschner. The bow produces traction as strong as necessary for the fracture. Held in place by a leather strip there is also applied through the forearm cuff a prop made of aluminum which is bent to fit the hollow of the hand. This prop produces light and comfortable dorsiflexion—the only physiological position of the wrist—whereas the fingers are slightly flexed.

The Kirschner wire is laid diagonally either across the basal phalanx of the finger to be extended in case of fracture of the metacarpal bones, or across the middle phalanx in case of fracture of the basal phalanx. We can report but the best results from the minor surgical operation which can be carefully carried out under local or nerve block anæsthesia without injury to any tendons, nerves, or arteries and without the danger of infection.

First the cuff, softly padded, the Kirschner wire, and the bow extension are put on. Then the fragments are placed in position after 2 per cent novocain has been injected into the hæmatoma to overcome pain. Now the wrist is slightly dorsiflexed and the fingers less so. After a few hours, the patient will be able to move the extended finger a little. The bandage is kept on for 2 or 3 weeks, which time is necessary for the consolidation of the fracture so that redislocation is made impossible. Then the usual treatment is followed: the application of warmth and massage and exercise of the hand and fingers.

By means of wire extension excellent results have been obtained during the past two years at the Surgical Clinic of the University of Frankfurt a. Main. With this method even extremely badly dislocated fractures which have been treated by other means without success are cured. The results have been very favorable from an anatomical as well as a functional point of view. In all the cases mentioned the time required for physical therapy has been considerable lessened compared with the time required, for instance, when the method of extension by adhesive plaster was used. As to the patient himself, this method is much more agreeable than are other ones, for it has the advantage of allowing a comfortable physiological position of the

Fig. 3.

Fig. 4.

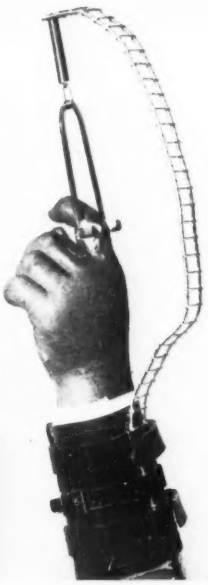

Fig. 5.

Fig. 3. Finger extension applied. Tennis racket form.
Fig. 4. Finger extension applied. Abduction position of the Kramer splint.
Fig. 5. Finger extension applied. Bayonet form of Kramer splint.

wrist and the joints without the patient being constantly reminded of his disability.

We believe that the postulates mentioned have been met by the wire extension apparatus and that this method may be recommended.

SUMMARY

An apparatus is described for the treatment of fractures of the fingers and metacarpal bones. The apparatus is based on the principle of wire extension. The apparatus permits more or less strong traction, bringing fingers and wrist into a comfortable middle position. The apparatus makes possible the correction and maintenance of exact reposition even in fractures with greatly dislocated fragments. The joints of the fingers can be moved without any pain immediately after the apparatus is applied—a means of facilitating the treatment afterward and a means of improving the results.

PANCREATIC LITHIASIS[1]

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SINCE the condition of pancreatic lithiasis was first described by Graaf in 1667, relatively few cases have been recorded. The rarity of the condition is evidenced by the fact that a careful search of the literature reveals only 107 cases. Opie, in 1910, found two cases in 1,500 autopsies at The Johns Hopkins Hospital.

It is probable that many cases are overlooked clinically, because of the great difficulty in recognizing the condition even with modern methods of investigation. This is well illustrated in the case about to be described. Furthermore, it has been recorded that stones have been missed at operation, even when suspected, and found at autopsy.

The literature on pancreatic lithiasis has been well reviewed from time to time. Oser, in 1900, collected 70 cases, and, 4 years later, Lazarus reviewed a total of 80 cases. In 1925, Seeger, in a comprehensive review, brought the total reported cases up to 101, including 1 case of his own. He emphasized the value of surgical treatment. Since Seeger's article appeared, reports of 6 more cases have been found; 4 by Hartmann, in 1925; 1 by Charvat and Felklova, in 1926; and 1 case by Lindsay, in 1929. The case about to be described brings the total up to 108. It is significant that, whereas almost all of the cases recorded up until the first of this century were autopsy findings, the greater number reported since have been operated on with, for the most part, good results.

We have studied all of the previously recorded cases, but, as the details of the earlier ones are scanty, it seems advisable to confine our analysis to the 54 cases reported since the middle of the last century, which are more complete. In analyzing these, striking differences between the group operated upon and the group of postmortem cases were noted in both symptoms and findings. For the sake of comparison, therefore, statistics of these two groups are presented separately. It will be noted, for example, that, whereas the average age in the postmortem series was 50 years, that in the surgical series was only 40 years. Of the entire 54 cases, 29 were surgical and 25 were reported as autopsy findings (Tables I and II).

Lindsay stresses the fact that both dull and colic-like pain are frequently present and that dull epigastric ache precedes the colic.

It will be seen from Tables I and II that epigastric pain of the colic-like type and, less frequently, epigastric pain, dull in character, is the predominating symptom. The radiation of the pain is variable. While in the majority of cases it is referred to the back, there is here no constant site of radiation; generally it is to one or other scapular region. In some cases, radiation as high as the shoulders has been noted, in others as low as the lumbar region. A number of writers, notably Seegar, have stressed left lumbar radiation. That this is characteristic, however, can hardly be accepted. Nausea and vomiting occur frequently in association with the paroxysms of pain.

Of greater importance than pain, from a diagnostic standpoint, is the frequent occurrence of

TABLE I.—SURGICAL CASES

Number of cases reported	(53.7 per cent)	29
Average age		40
Sex		
Males		10
Females		17
Not mentioned		2
Symptoms and Signs		
1. Pain		
Dull epigastric		5
Colic-like epigastric		19
Absent		2
Referred to thoracic region of back		8
Referred to left lumbar region		4
Referred to both lumbar regions		1
Radiating down ureter (left)		1
Reference not mentioned		3
2. Nausea and vomiting with attacks of pain		7
3. Glycosuria (always late)		4
4. Jaundice with attacks		8
5. Steatorrhœa		6
6. Diarrhœa with attacks		3
7. Stones in the stool		2
8. Marked loss of weight		10
9. Irregular pigmentation of skin		2
10. Palpable tumor		2
11. History of duodenal ulcer		2
12. X-ray findings		
Positive pre-operative		2
Positive postoperative		2
Negative		1
Findings		
1. Calculi		
Multiple		23
Single		6
2 Cysts of pancreas		1
3. Abscess of pancreas		3
4. Fat necrosis of pancreas		1
5. Carcinoma of the pancreas		1
Associated Findings		
1. Duodenal ulcers		3
2. Gall stones		4
Results		
1. Immediate recovery	(92.6 per cent)	27
2. Postoperative deaths	(7.4 per cent)	2

[1] From the Department of Pathology, The Montreal General Hospital, and The Ste. Anne's Military Hospital.

steatorrhœa and diarrhœa. The occurrence of steatorrhœa and the rare finding of typical calculi in the stools, emphasize the importance of a careful examination of the fæces. Kinnicut, in 1903, reported 7 cases, including 1 of his own, in which the diagnosis had been established from examination of the fæces.

Glycosuria has been reported in a large number of cases, particularly in the postmortem group. Oser, in his series of 70 cases, found that it occurred 22 times, while Lazarus notes its occurrence in 36 of his 80 cases. Opie points out that this condition comes on late in the disease, after fibrosis of the pancreas has become so extensive as to involve the islets of Langerhans. Glycosuria does not necessarily mean, however, that surgical intervention will not still relieve and even cure the condition, as will be noted in the included statistics.

Loss of weight to a marked degree occurred frequently enough to attract attention.

In 14 of the cases (about 25 per cent), obstructive jaundice led to the incorrect diagnosis of gall stones in the common duct. Jaundice is due either to obstruction at the ampulla of Vater by an extruded pancreatic calculus, or to pressure upon the common duct by inflammatory swelling or stone in the head of the pancreas.

Associated pulmonary tuberculosis was found in 6 cases and in the case here reported. Its occurrence, however, can hardly be said to be more frequent than the association of pulmonary tuberculosis with diabetes mellitus generally. In only 1 case, that of Bissell, was a tuberculous lesion found in the pancreas.

TABLE II.—POSTMORTEM CASES

Number of cases reported (46.3 per cent)	25
Average age	50
Sex	
Males	14
Females	6
Not mentioned	5
Symptoms and Signs	
1. Pain	
Dull epigastric	4
Colic-like epigastric	12
Absent	3
Not mentioned	6
Referred to thoracic region of back	5
Reference not mentioned	20
2. Nausea and vomiting with attacks of pain	7
3. Glycosuria (always late)	10
4. Jaundice with attacks	6
5. Steatorrhœa	6
6. Diarrhœa with attacks	5
7. Stones in the stools	3
8. Melæna	1
9. Distention	2
10. Marked loss of weight	6
11. Irregular pigmentation of skin	2
12. X-ray findings (none mentioned)	0
Findings	
1. Calculi	
Multiple	24
Single	1
2. Pancreatic cysts	2
3. Abscess of the pancreas	2
4. Tuberculosis of the pancreas	1
Associated Findings	
1. Gall stones	2
2. Duodenal ulcers	2
3. Pulmonary tuberculosis	6

Fig. 1. Roentgenogram showing calculi in the pancreatic duct. (From the X-ray Department of The Royal Victoria Hospital, Montreal.)

The finding of gall stones in 4 cases and pancreatic carcinoma in 1 case may be considered in the light either of cause or effect, or as purely coincidental, the latter explanation applying with added force to the 3 cases showing duodenal ulcer.

In but 4 cases have pancreatic cysts been found, and the explanation given by some writers is that the duct of Santorini has been present and has remained patent.

The pancreatic stones are almost invariably located in the ducts. Seldom are they found embedded in the parenchyma of the gland. It has been noted that they do not tend to lodge in the terminal portion of the duct of Wirsung as it passes through the duodenal wall. The ducts behind the stones eventually become dilated, and in addition to the stones may also contain grumous material. The pathological changes in the parenchyma of the gland are characteristic. First, there develops an interlobular pancreatitis with small round cell infiltration and, later, fibrosis. The fibrosis gradually extends and eventually involves the whole parenchyma in a diffuse way, compressing the acinar tissue. Pressure from dilated ducts undoubtedly plays a part in this destructive process. As Opie has stressed, the islets of Langerhans are

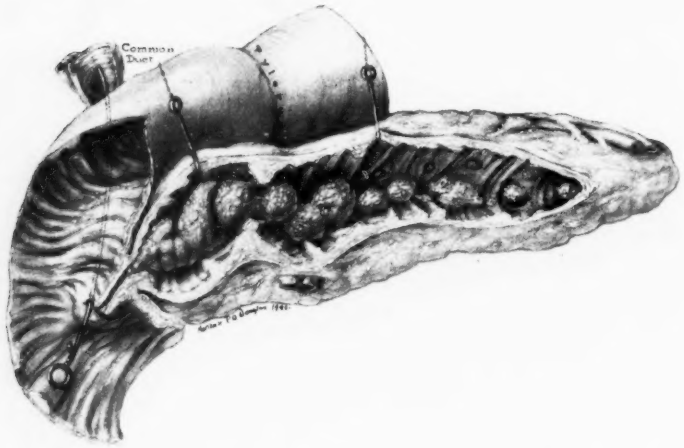

Fig. 2. Drawing showing the pyloric end of the stomach, a portion of the duodenum, the pancreas, and adjoining tissues. Note the stones in the opened dilated pancreatic duct and tributaries. Probe in the common duct.

the last to become involved. The calculi have been described as varying from a pale yellow to a light grey in color. They are usually quite friable. They vary in size from sand-like particles to one described by Schuppmann measuring 1½ inches in diameter. They are rough, irregular, sometimes jagged, and the larger ones may even take on a stag-horn appearance, from projections into dilated branch ducts. When multiple large stones are present they are often facetted, as in the case about to be described. In cross section they show no definite concentric formation, but are seen to contain organic material. Chemical analysis has been found to be substantially the same in all instances. Calcium carbonate and calcium phosphate form the chief constituents. Barron, who investigated this matter particularly, found that there also occurred, less frequently, small quantities of other phosphates and occasionally traces of cholesteral, magnesium carbonate, and calcium oxalate.

Regarding the causation of stone formation, all the accumulated evidence points to a primary inflammatory condition, with stasis as a secondary factor. Not only do the accompanying pathological changes in the pancreas bear this out, but the composition of the stones themselves offers additional evidence. Normal pancreatic secretion, it has been shown, does not contain calcium salts. On the other hand, it is well known that calcium salts are always found in excess in any inflammatory process. Just as calcium deposition in gall stones is secondary to an inflammatory lesion, so it occurs also in pancreatic stones.

The following is an abstract of a case which came to autopsy at Ste. Anne's Military Hospital, Ste. Anne de Bellevue, Quebec. The history is based on records kindly supplied by St. Bartholomew's Hospital, London, England; The Boston City Hospital, Boston, Massachusetts; The Victoria General Hospital, Halifax; The Royal Victoria Hospital, Montreal; and the Ste. Anne's Military Hospital.

K. D., male, aged 57 years, British born, a civil engineer by profession, was admitted to Ste. Anne's Military Hospital on May 1, 1929, in a dying condition.

From the age of 2 to the age of 8 years he had had discharging sinuses in his neck, probably tuberculous in origin. In 1904, he first complained of attacks of upper abdominal colic-like pain accompanied by nausea, vomiting, and loss of weight. These attacks were aggravated by taking food. He was admitted to St. Bartholomew's Hospital, London, the same year. At an exploratory operation a nodular mass found in the pyloric region was thought to be carcinoma of the pylorus and a gastro-enterostomy was performed. The patient was considerably relieved for a few months, when the attacks again recurred occasionally, but not so severely. After coming to Canada, 1911, he contracted typhoid fever and received treatment in The Victoria General Hospital Halifax, for 6 weeks. In 1912 he was admitted to The Boston City Hospital, because of the return of the attacks of abdominal pain. He was treated with laxatives and enemas for 5 days and then discharged, relieved.

In 1915, 11 years after the abdominal operation, he enlisted in the Canadian Army and went overseas. While in England he was treated in a military hospital for abdominal colic and vomiting. He continued to have recurring attacks of a similar nature while overseas. In 1919, he returned to Canada.

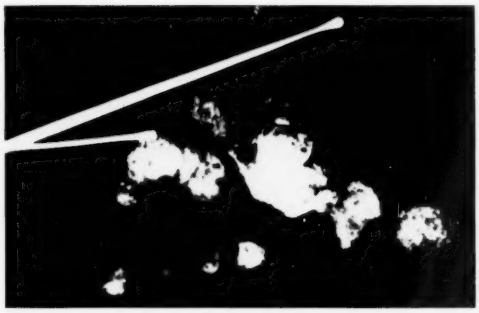

Fig. 3. Roentgenogram of the fresh pathological specimen shown in Figure 1, with a probe in the common bile duct and another in the pancreatic duct as far as it could be inserted. Note the multiple stones in the pancreatic duct.

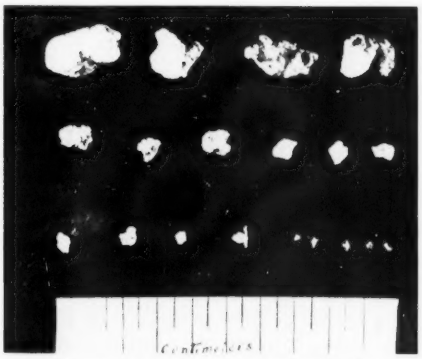

Fig. 4. Stones removed from the pancreatic ducts showing various sizes and shapes; facetting is indistinctly seen.

In 1920 he first noticed frequency of urination and a craving for sweets. The following year he developed a definite polyphagia. In 1923, he had a severe recurrence of epigastric colic and vomiting. He found that vomiting relieved his pain and he frequently sought relief by inducing it. The same year, he was admitted to the Victoria General Hospital in Halifax for these symptoms. There, for the first time, glycosuria was noted. In 1924, he again entered the same hospital on account of abdominal pain. Glycosuria was again found. It should be noted that he was disinclined to follow his dietary instructions, and, moreover, was addicted to the use of alcohol. In 1925, thirst and polyuria became more marked. In March, 1926, he attended the Boston City Hospital Clinic, complaining of pain in the left shoulder. A diagnosis of diabetes mellitus and alcoholic neuritis was made. In April, he was again admitted to the same hospital on account of his abdominal symptoms. Here it was recorded that he was addicted to the use of veronal as well as alcohol. Not long after this, in 1926, his abdominal symptoms entirely cleared up and never recurred. In August, 1927, he developed a cough and began to lose weight rapidly. He had hæmoptysis on two occasions during that month. Again entering the Boston City Hospital, pleurisy was found as well as his diabetic condition. Insulin was used for the first time, and on leaving the hospital he was taking a dosage of 20-0-20 units. He continued to lose weight steadily and his cough persisted. By February, 1929, he had lost 44 pounds.

On February 9, 1929, he was admitted to The Royal Victoria Hospital, Montreal, where the diagnosis of chronic pulmonary tuberculosis was added to that of diabetes mellitus.

Laboratory findings. Urinalysis showed urine, acid; specific gravity, 1.037; sugar, +++; albumen, +; acetone, trace; bile, 0; microscopic pus cells, scattered and in clumps. Blood count showed red blood cells, 4,140,000; white blood cells, 9,000; hæmoglobin, 90 per cent. Blood Wassermann was negative. Blood chemistry: urea, creatinine and cholesterol, normal values. Gastric analysis: normal findings. Stool examination: nothing unusual noted. Barium series showed a well functioning gastro-enterostomy. Shadows were noted at the level of the first and second lumbar vertebræ, suggesting calcified glands. These have since been identified as pancreatic calculi (Fig. 1). X-ray examination of chest confirmed the diagnosis of pulmonary tuberculosis. The Tipp test showed a pathological gall bladder. Cystoscopic examination, with a pyelogram gave negative findings.

The patient's pulmonary condition became rapidly worse and on May 1, 1929, he was transferred to Ste. Anne's Military Hospital, where he died May 9.

Abstract of postmortem findings. The pancreas was buried in dense fibrous adhesions and was very much atrophied. Part of the adhesions were intimately associated with the gastrojejunal stoma. On palpation the pancreas was hard and fibrotic. Along the course of the duct of Wirsung several large stones could be felt which gave distinct crepitation. Gross sections of the gland showed this duct to be widely dilated throughout and filled with numerous greyish-white stones of various sizes and shapes. While some were rough and irregular, the larger ones were facetted at contact points. Branches of the main duct were also dilated and contained many similar though smaller stones (Fig. 2). In addition to the stones, the ducts also contained yellowish, grumous material and sand-like particles. The duct walls were all greatly thickened and the parenchyma almost entirely replaced by fibrous tissue. An X-ray picture of the extirpated pancreas was made (Fig. 3), and this revealed the presence of many small stones in remote parts of the gland. These were afterward found to lie in dilated ducts. Some of the more accessible calculi were removed and photographed (Fig. 4). Chemical analysis of these stones showed the chief constituent to be calcium carbonate, with a smaller amount of calcium phosphate.

In addition, there was extensive ulcerative tuberculosis of the upper lobe of the left lung and bilateral pleural effusion. There was also an empyema of the appendix; the kidneys showed cloudy swelling; and the spleen an acute hyperplastic condition.

Microscopic examination of the pancreas. Many sections taken from various parts of the gland all showed marked loss of glandular tissue with extensive replacement fibrosis. In some areas the latter contained considerable small round cell infiltration. What acinar tissue remained was present only in small islands, and these showed postmortem autolysis. Acinar tissue was relatively best preserved in the sections from the head, but even here it was very far from normal. In none of the many sections could normal, or even nearly normal, islets of Langerhans be recognized, but here and there, embedded in the fibrous connective tissue indistinct remnants of these were seen (Figs. 5 and 6). The duct walls generally were greatly thickened by fibrous connective tissue, while sections through the terminal portion of the duct of Wirsung and common bile duct just above the ampulla showed, in addition to this thickening, considerable surrounding fibrosis and small round cell infiltra-

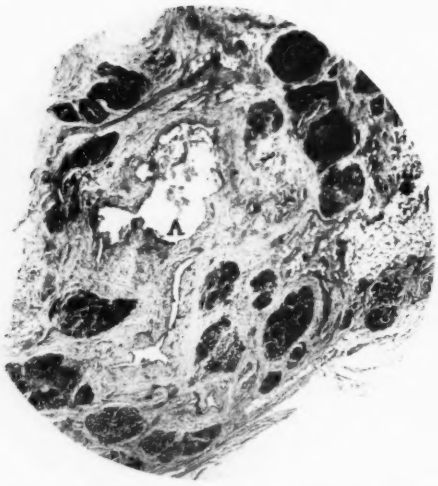

Fig. 5. Low power photomicrograph of pancreatic tissue. The darker areas are islands of pancreatic tissue; the lighter, dense fibrous tissue. A dilated pancreatic duct is seen at A.

Fig. 6. High power photomicrograph showing the extensive fibrosis in the pancreatic tissue, with a small island of degenerated residual acinar tissue.

tion (Fig. 7). There was considerable peripancreatic inflammatory connective tissue which involved also the adjacent lymph nodes.

This case illustrates well the difficulty of making an accurate diagnosis of pancreatic lithiasis, even with roentgen-ray assistance. This difficulty is attested to by all writers, but on the other hand, the more recent statistics certainly show a decided improvement. Not only have a larger number of definite pre-operative diagnoses been made than formerly, but in a still greater number of cases have calculi been suspected and their presence confirmed at operation. Because of earlier recognition and treatment relatively fewer cases with glycosuria have been recorded in recent years. In some cases, even on direct palpation of the pancreas, a simple stone may be difficult to locate especially if extensive fibrosis be present. On the other hand, attention has been called, especially by Link and Sistrunk, to a peculiar crepitus that exists when there are multiple stones. The value of the roentgen-rays in the diagnosis has been particularly stressed by Mayo-Robson, especially in view of the composition of the stones. Hartig, however, describes a case in which X-ray examination was negative, but several large stones were found at operation. On the other hand, Lindsay's 2 cases both showed suggestive shadows, and in his more recent case this writer felt that this examination definitely confirmed the diagnosis. Lacoutre and Charbonnel X-rayed their patient after operation only, when several overlooked stones were seen. In a few instances, including our case, however, the shadows have been mistaken, as can readily be understood, for calcified glands which are commonly found in this region. In at least two cases the X-ray diagnosis of renal calculi has been made.

Fig. 7. Photomicrograph (planar) of a transverse section through the ampulla of Vater, showing the common bile duct *A* and the patent pancreatic duct *B*.

OPERATIVE TREATMENT

The excellent results that have attended operation in recent years deserve special emphasis. Not only have the end-results been gratifying, but the mortality rate is satisfactorily low, being approximately 6.5 per cent. It is notable that in neither of the two deaths following operation did either fat-necrosis or peritonitis occur; in none of the cases did a permanent fistula develop. The secret of this, as Seeger has pointed out, is adequate drainage, preventing retroperitoneal accumulation of pancreatic secretion. All of the 7 cases reported with glycosuria previous to operation recovered. In 4 of these a definite postoperative improvement in sugar tolerance is recorded.

Various avenues of approach to the pancreas have been described. In general, however, the route chosen has depended on the location of the stones. When these are located in the head of the gland some surgeons, notably Sistrunk, have favored retracting the second part of the duodenum medially and thus reaching the pancreas from behind. Dalzeil, in 1902, reported a case in which he successfully removed four stones from as many different parts of the gland. Moynihan and others have opened the duodenum and removed stones through the ampulla. Hartig's case had an associated carcinoma of the head of the pancreas from which the patient died 5 months later. To discuss the relative merits of the different operative procedures does not come within the scope of this paper. One is content to stress the gratifying results that have attended the surgical treatment of this condition since Caparelli, in 1876, reported the first case successfully operated on.

SUMMARY

1. Pancreatic lithiasis is a comparatively rare condition, there having been only slightly over 100 cases reported.

2. Whereas most of the earlier cases reported were from autopsy findings, the majority in the last 50 years have been successfully operated on.

3. Epigastric pain of both dull and colic-like nature is the commonest symptom, but unfortunately there is no consistency in radiation.

4. Steatorrhœa and diarrhœa attract particular attention in the symptomology. These symptoms, together with the occasional finding of calculi in the fæces, make the examination of the stools of great importance.

5. Glycosuria of true diabetic character is a frequent finding late in the condition. It appears to be coincident with extensive destruction of the islets of Langerhans by the fibrotic pancreatitis which occurs with this condition.

6. Jaundice occurs often enough to lead frequently to the incorrect diagnosis of cholelithiasis.

7. Correct clinical diagnosis is difficult, and though the roentgen-ray is of great value it may, as in our case, not be conclusive, while even at operation stones may be missed, particularly if single. A peculiar crepitus when multiple stones are present has been described.

8. Surgical treatment has yielded very gratifying results from every standpoint. The mortality rate is less than 6.5 per cent. When properly treated the presence of diabetes mellitus does not constitute a contra-indication to operation.

9. Characteristic pathological changes occur in the parenchyma of the gland, beginning as a chronic interlobular pancreatitis and gradually involving the whole gland in a fibrotic process, with resultant atrophy and loss of parenchyma. The islets of Langerhans are last to be involved.

10. The calculi are composed for the most part of calcium carbonate and calcium phosphate. These findings are suggestive of an inflammatory etiology.

11. Associated pulmonary tuberculosis has been noted in a number of cases. The incidence of this is, however, probably not more than might be expected in diabetes mellitus generally.

12. A typical case is reported with a history of 25 years, and with the autopsy findings. Glycosuria was present during the last 5 years of the condition and active pulmonary tuberculosis only during the last 6 months.

BIBLIOGRAPHY

1. Barron. Surg., Gynec. & Obst., 1920, xxxi, 437.
2. Bissell. Tr. Chicago Path. Soc., 1913–1915, ix, 167.
3. Caparelli. Ref. Guidiceandrea, Policlin., Rome, 1876.
4. Charvat and Felklova. Časop. lék. česk. Praha, 1925.
5. Dalzeil. Brit. M. J., 1902, ii, 312.
6. Hartig. Med. Klin., 1915, xii, 166.
7. Hartmann. Ann. Surg., 1925, lxxxii, 956.
8. Kinnicut. Am. J. Med. Sc., 1902, N. S. cxxiv, 948.
9. Lacoutre and Charbonnell. Rev. de chir., 1914, i, 28.
10. Lazarus. Beitrage zur Pathologie und Therapie des Pankreas mit besonderer Berucksichtgung den Cysten und Stein. Berlin, 1904.
11. Lindsay. Lancet, 1922, ii, 612.
12. Link. Ann. Surg., 1911, liii, 768.
13. Mayo-Robson. Lancet, 1904, i, 911.
14. Moynihan. Lancet, 1902, ii. 355.
15. Murray. Proc. Roy. Soc. Med., 1911, v, 131.
16. Opie. Diseases of the Pancreas. Lippincott: Philadelphia, 1910.
17. Oser. Nothnagel's Special Pathology and Therapeutics.
18. Schuppmann. Cited by Oser.
19. Seeger. Surg., Gynec. & Obst., 1925, xl, 841.
20. Sistrunk. Ann. Surg., 1921, lxxiv, 380.

KNOTTING OF THE UMBILICAL CORD

With a Report of Two Cases and Illustrations of the Mechanism of Knot Formation

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IN human beings the umbilical cord is subject to many kinds of torsion, coiling, looping, and knotting during pregnancy or during parturition. Torsion of the cord is a common occurrence. In a case recently admitted to the hospital the umbilical cord of the aborted fetus of 4 months' pregnancy was twisted ninety-one times (Fig. 1). DeLee records a case in which the death of the fetus might have resulted from stricture of the cord which was twisted 380 times. There is the remote possibility that the activity of fetal death agony may produce the torsion or that the cord may become twisted after the child's death by uterine contractions. In the latter case no adhesions would be found between the coils of the cord and when untwisted the shape of the cord would not be permanently altered.

Coiling about the neck or body of the fetus has been found in 25 per cent of the cases, but knotting of the cord in only 0.5 per cent. Von Winckel considers the occurrence of knotting of the cord rare, being found in not more than 0.4 to 0.5 per cent of all births. Chantreuil found seven knots of the cord, six simple and one double, in 1,000 deliveries. Von Hecker records 31,590 births in which he found true knots of the cord 116 times, a ratio of 1 to 274 births.

Such anomalies are not characteristic of the lower animals, however. Torsion has been discovered in about 40 per cent of cases, chiefly in horses and pigs. Seldom has the cord been coiled or looped about the neck of the offspring and never has a knotted cord been observed. Sellheim ascribes the greater occurrence of twisting and knotting of the cord in human beings to their upright posture, their ability to swing about rapidly on a vertical axis, the heavy head of the human fetus as compared with the body, and to the fact that it must remain longer in bent position before reaching the pelvic outlet. The theoretical transmission of the effect of physical motion of the mother on the contents of the uterus has led one writer to regard these multiple high grade torsions and knots as the automatic registering apparatus of outside stimuli on intra-uterine life. Schneider offers the hypothesis that the knots are formed in the developmental stage at the time when the body stalk is fusing with the omphalomesenteric duct as it passes into the amniotic cavity when the embryo is about 5 millimeters in length. Most authorities believe, however, that the most favorable time for knot formation during pregnancy is from the ninth to the twelfth week of intra-uterine life. At this time the fetus is very small and is swimming about in an abundance of amniotic fluid. Contributing factors are an extremely long cord, hydramnios, exaggerated fetal movements, or violent movements on the part of the mother. It is evident that a long cord and a great amount of amniotic fluid will facilitate fetal movement. But authors have reported finding knots in very short cords: Collyns found two knots in an umbilical cord which measured only 6 inches. Such cases are exceptional.

The formation of a single true knot is a formidable process which is influenced by contractions of the uterus, passivity, and subsequent sudden activity on the part of both mother and fetus, and the laws of gravitation. The fetus itself may slip through the loop, or the loop may accidentally fall over the head of the fetus. The first stage in the process is torsion, which is due to a simple twisting of the fetus on the axis of the umbilical cord. The mechanics is similar to that involved when the pedicle of an ovarian cyst becomes twisted. If the torsion is prolonged, a coil or loop may be formed. If a particular movement or series of movements then drives the loop toward the fetus or the fetus toward the loop and the fetus reverses its motion, diving through the coil, a variety of knots may result. Experiments with weights and strings have revealed a chaotic number of possibilities of knot formation.

The situation of the knot often may be used as an indicator to mark the time of its formation. If the knot is formed early, it will be close to the navel; if late, it will be at the placental end. McCaffrey, however, discovered through experimentation that a pressure equal to that exerted by the pumping of the fetal heart has made the knot travel 6 inches along the cord, so that this method is not impeccable.

Discrimination between knots formed during pregnancy and those resulting from labor can ordinarily be made with little effort. Sellheim noticed that knots found in premature fetuses

were firm whereas those formed during parturition always had a perceptible response when pulled and had retained elasticity. Browne observed that knots formed early in fetal life are flattened out and bandlike. When these knots are untied there is left a grooving in the cord which curls involuntarily and the jelly of Wharton has disappeared at the site. The vessels are compressed, of diminished caliber, and the vessel walls hypertrophied. The section of the cord proximal to the knotted area is often œdematous, the other end thin, tenuous, and pale. Recent knots of parturition, as when the cord becomes coiled around the *os uteri* and the infant is drawn through the loop or when the fetus passes through a loop spread out in the lower uterine segment, show no anatomical changes, except possibly a little œdema on the fetal side of the cord.

ILLUSTRATIVE CASES

CASE 1. V. C., female, white, 34 years of age, who had previously given birth to two children, was delivered at full term of a normal male child weighing 10 pounds, 3 ounces. The pregnancy was uneventful. Fetal life was normal. Ten days prior to admission to the hospital some pain had been felt with unusual fetal activity which decreased without much perceptible motion since this time. At birth the cord was found to be tied in a knot of the type illustrated in Figure 2, commonly called a lover's or sailor's knot.

The mechanism of the formation of such a knot admits of two possibilities:

Method A, Figure 4: *1*, The fetus is pictured in the uterus in upright position. The cord has formed a noose at one side of the fetus and part of the cord is draped over the left shoulder with the placental end crossed over the fetal end. *2*, The fetus dives forward so that the fetal end of the cord passes over his head and the placental end beneath his chin. *3*, The somersault of the fetus is half complete. The head is beginning to pass through the loop. *4*, The fetus is twisted slightly. The head and shoulders have passed through the loop. *5*, The fetus is through the loop and again in upright position. The knot formed is a lover's or sailor's knot.

Method B, Figure 5: *1*, The fetus is in upright position with two strands of the cord passing in front of the fetus and a loose coil at the left side. *2*, The fetus has made a half-twisting of the body toward the loop with the placental end of the cord lying over the fetal end. *3*, The fetus has turned completely around forming a second coil about the body. *4*, The fetus somersaults forward passing head first through coil and loop. *5*, The somersault is half complete. *6*, The knot is completed, being the same type of knot as that formed by method A.

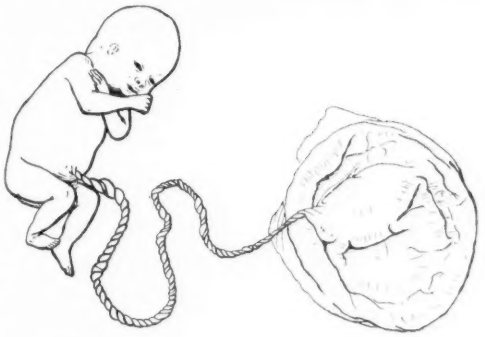

Fig. 1. Umbilical cord of fetus of 4 months' pregnancy presenting 91 twists.

CASE 2. R. B., female, white, 42 years old, gave birth to male twins by spontaneous delivery May 30, 1930. One twin weighed 6 pounds, the other 6 pounds, 5 ounces. They were similar twins in the same amnion without dividing septum, born by breech presentation. The membranes ruptured before admission to the hospital. X-ray of the abdomen on May 28 showed the presence of twins in the uterus. At this time the fetal heart beat was perceptible. Pregnancy was uneventful. At delivery it was discovered that the umbilical cords were intricately knotted.

Twins in one amnion often have intertwined cords but rarely intricate knotting. Figure 3 shows the knotting and intertwining of the cords of these uniovic twins.

The effect of the knotting of the umbilical cord on the life of the fetus has been the subject of much controversy. Guinness reports a case in which a knot in the cord caused acute hæmorrhage. The mother during the second pregnancy and just before parturition was seized with continuous but not severe hæmorrhage. No signs of placenta prævia were present. No fetal heart sounds were audible. After the vagina was tightly packed the child was stillborn in vertex presentation followed by blood clots and placenta. The cord, longer than the average, contained a single complete knot which blocked fetal circulation and caused the separation of the placenta and hæmorrhage before labor set in. Some days previous to entrance the patient had complained of great fetal activity which suddenly ceased.

Kittler reports a case in which a woman strained herself during the third month of pregnancy by reaching for a door knob to save herself from falling. She was delivered prematurely during the seventh month. About the body of the dead fetus was a lasso knot so tightly drawn that the abdomen bulged markedly above and below the cord.

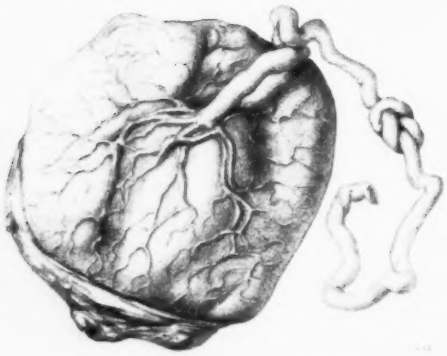

Fig. 2. Umbilical cord tied in a sailor's or lover's knot.

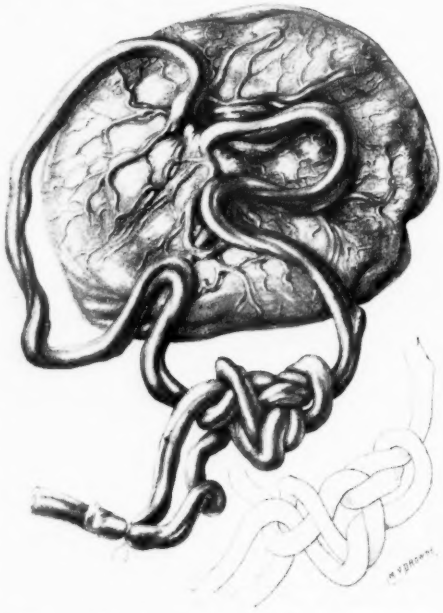

Fig. 3. Knotting and interlacing of cords of similar uniovic twins.

An interesting case of knotting of the cord without injury to the child is one reported by Fleming. A woman, 28 years of age, was delivered at full term of a large, healthy boy. The cord contained two knots, one a figure-of-eight located about one foot from the placental end, the other a single knot at about the same distance from the umbilical end. The cord was 4 feet long and both knots were loosely tied. Fleming had discovered single knots in the cord in previous cases but never two knots in the same cord. In von Hecker's 31,590 cases there were 115 instances of cord knotting and in no case had the knot affected the child's development in any way. McCormick delivered with low forceps a primiparous patient. The baby was fully developed and unasphyxiated. The cord presented a knot in the form of a rather loose figure-of-eight. In the prenatal history there was only one possible cause of the knotting of the cord: at 7 months' gestation the patient had fallen, the effects of which necessitated hospitalization for five days.

From the few cases in the literature it may be inferred that knotting of the cord has caused the death of the fetus in about 50 per cent of occurrences. Knots formed during delivery are almost never serious. If knots are formed in early gestation, they are more apt to prove fatal by traction on the cord producing asphyxia. Sometimes they may be tight enough to interfere with the development of the fetus when the constant pulsation of the cord and the resulting turgescence may prevent a tightening of the cord to the point of asphyxiation. Certainly if the knots are slack they have no effect on fetal development, and von Winckel believes that they can never be drawn tightly enough to interfere with the circulation until labor begins. Baudelocque found in one cord two double knots so tightly drawn that when the cord was finally untied a deep groove remained at the site of the knot, yet the child was normal. Chantreuil affirms that tight knots can cause death or emaciation of the fetus from undernourishment.

To throw some light on the problem, Tannier performed an interesting experiment. He made a knot in an umbilical cord and pulled it as tightly as possible. Then he pumped fluid into the cord. He found that fluid would always pass through the knot, which partially untied itself when the vessel in front of the knot became swollen enough to exert pressure on the cord. He came to the conclusion that the fetal heart could in every instance exert a degree of pressure sufficient to maintain the fetal circulation.

Browne went a step farther with the same sort of experimentation. By applying different weights and pressures to the knotted cord he showed that under certain conditions more pressure was required to force the fluid through the knot and that this pressure was greater than the fetal heart could exert; he concluded, therefore, that in some cases a knot did interfere with and even completely obstruct cord circulation.

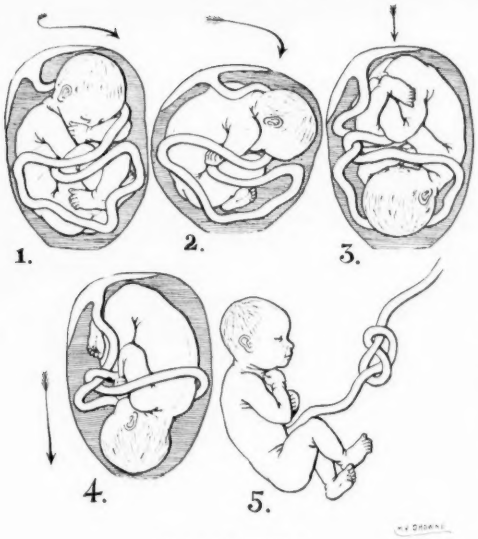

Fig. 4. Method A.

Fig. 5. Method B.

The separate cords of twins provide excellent opportunities for unusual twisting, interlacing, and knotting, especially when the two fetuses are encased in one amnion without a dividing septum. Rossier reports a case with excellent illustrations of univitelline twins whose cords were interlaced and intricately knotted. Sonntag collected 23 cases of entwined and knotted cords in single amnion pregnancy. In 2 cases only, both of the twins lived. In 1 of these 2 cases the cords were both twisted and knotted, in the other, merely knotted. In 5 cases 1 of the twins lived and was born at term; in 4 of the cases both interlacing and knotting were present. The rest of the cases, 16 in number, were miscarriages at from 4 to 5 months, in which all but two of the cords showed interlacing and knotting; in these two, knots only were formed. Freund reports a case of mono-amniotic twins who died after 6 months' pregnancy. One cord longer than the other had encircled the shorter one three times and then looped itself over it to form a single knot. The first circling of the cord was so tight that the cord was compressed markedly. According to Rosenburger, one mono-amniotic twin pregnancy occurs in 60,000. Sachs reports a case of five knots in the cords of twins in one amnion and calls the condition extremely rare. Gornick reports finding many conglomerate knots in the cords of mono-amniotic twins of 8 months' pregnancy. The female child was delivered first, badly asphyxiated. The second child, male, could not be revived, its respiration being cut off by the torsions and knottings. The author stated that in only 4 of 16 cases in his experience were the twins born alive. In 7 cases one child lived, and in 5 both died. Kauffmann reports the spontaneous birth of living male twins in a single amnion with no separating membrane, whose cords were tied in a double sailor's knot.

In his report of 3 cases of death of the fetus owing to abnormalities of the umbilical cord, King makes the suggestion that more such cases be reported. In this way it will become possible to arrive at a more accurate estimate of infant mortality from this irremediable anomaly.

BIBLIOGRAPHY

1. Browne, F. J. J. Obst. & Gynæc. Brit. Emp., 1925, xxxii, 17.
2. Chantreuil, A. Thèse de doct., Paris, 1875.
3. DeLee, J. B. The Principles and Practice of Obstetrics, p. 570. Philadelphia, 1915.
4. Fleming, H. C. Texas State M. J., 1924, xix, 579.
5. Freund, R. Ztschr. f. Geburtsh. Gynaek., xcvii, 100.
6. Guinness, A. F. G. Brit. M. J., 1922, i, 875.
7. King, E. L. Am. J. Obst. & Gynec., 1926, xii, 812.
8. Kittler, E. Zentralbl. f. Gynaek., 1928, lii, 1717.
9. McCaffrey, L. E. Am. J. Obst., 1927, xiii, 104.
10. McCormick, C. O. J. Indiana M. Ass., 1929, xxii, 245.
11. Rosenburger, Gornick, and Kauffmann. Cases reported by R. Freund, loc. cit.
12. Rossier, G. Schweiz. med. Wchnschr., 1926, lvi, 722.
13. Sellheim, H. Zentralbl. f. Gynaek., 1922, xlvi, 1746.
14. Sonntag. Quoted by S. F. Abrams. Am. J. Obst. & Gynec., 1921, i, 955.
15. Tannier. Quoted by Browne, loc. cit., p. 19.
16. Von Hecker. See Browne, loc. cit., p. 17.
17. Von Winckel. Quoted by F. J. Browne, loc. cit., p. 17.

ELECTROHÆMOSTASIS IN PLACE OF LIGATURES

Presentation of a Small, Simple Apparatus for Electrocoagulation[1]

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THE use of the high frequency electrical current, which was introduced into medicine some 25 years ago, received its greatest impetus from urologists, who have demonstrated its great usefulness, particularly in the treatment of vesical tumors. This work, which has revolutionized intravesical neoplastic surgery, led to a further development known as diathermy, which has been applied to practically all branches of medicine and surgery. Then came another development of electrosurgery, the electric scalpel, and numerous articles have appeared from enthusiasts, who have predicted a rapid replacement of the cutting scalpel. As a result of intensive experimental work by Bovie and others, the range of current and extension and usefulness of high frequency electrosurgery have been greatly increased, and in the past 2 years the literature on this subject alone has filled many pages of the medical journals here and abroad. Leaders in the profession have come forward to approve of its use in almost every type of surgery. A mention of the various articles is impossible, but we may refer in passing to papers by Harvey Cushing and Charles A. Elsberg on electrosurgery in the removal of intracranial tumors, Matson on the cauterization of adhesions in artificial pneumothorax, F. M. Mikells on the treatment of lesions of the cervix, L. Davis and B. N. Groen on its use in neurological conditions, H. E. Mock in thyroidectomy, G. A. Wyeth in various neoplastic lesions, Howard A. Kelly, John Anderson, and G. E. Ward, and others in general surgery, particularly the surgery of very hæmorrhagic organs, such as the liver, spleen and kidney, and finally A. J. McLean, who has discussed the underlying principles and results obtained by the Bovie electrosurgical current generator. Most important is the recent book by Kelly and Ward. Of great interest has been the development of various modifications of my prostatic "punch" with different types of electrocoagulation and cautery. In these various papers it has been demonstrated that comparatively bloodless surgery could be carried out rapidly and effectively by electrosurgery.

I have been greatly impressed with the value of electrosurgery in arresting hæmorrhage, particularly in the cortical bleeding which occurs in the kidney and in the replacement of ligatures where possible. I have not been convinced that in the ligation of blood vessels of any size electrosurgery should be used instead of the safe and certain methods of ligation. But in extensive operations which would ordinarily require great numbers of ligatures from small bleeding points, the value of electrosurgery is great, if the technique adopted is such as to leave a minimum amount of destructive tissue change. Ligatures themselves are recognized as distinct impediments to perfect wound healing. Years ago Dr. Halsted was most insistent on the great advisability of picking up with artery clamps very small bits of tissue for ligation, and the avoidance of mass ligation, which leads to the necrosis of large areas of tissue and consequently endangers proper wound healing. To minimize the amount of tissue clamped and ligated, he brought out the pointed Halsted clamp and subsequently the mosquito clamp, with which very small amounts of tissue are picked up and ligated. By means of his very careful hæmostatic methods and the avoidance of mass ligation, Halsted had been able to obtain perfectly dry wounds, discarding drainage tubes and thereby obtained perfection in closure and healing which had rarely been accomplished before. The great advantage of complete hæmostatis, as insisted upon by Dr. Halsted, has been abundantly proved. The one disadvantage has been the considerable lengthening of the operative procedure as a result of such meticulous care. When it is possible for the surgeon to proceed with his operation, the bleeders on each side of the wound being rapidly caught and clamped by expert assistants, little or no delay is encountered until the time for ligation of the bleeding points occurs. Here one is often uncertain just what points need ligation, and which clamps may be safely removed without a ligature. As a matter of fact, the mere compression caused by a clamp, which has remained *in situ* for some time, is often sufficient for hæmostasis. The importance of avoiding large numbers of ligatures is self-evident. With a wholesale removal of clamps numerous bleeders are encountered, the wound becomes stained and subsequent placing of clamps and ligatures is time consuming. The advantage of some method

[1] From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

by which hæmostasis could be obtained without the placing of ligatures, and at the same time without injury of the tissues is obvious. For this purpose the application of the high frequency electrical current has shown great possibilities, but as already stated, it must be done so lightly and delicately as to do nothing more than to cause sufficient adhesion of or alteration in the tissues to prevent opening up of the bleeding points, and at the same time to avoid necrosis sufficient to impair or retard wound healing.

In the development of the wonderful apparatus which has gone on apace, various types of current and variations of intensity are now afforded, so that if the operator will take the trouble to master the subject, he has at hand a great opportunity for the useful employment of electricity in his surgical work.

With the constantly changing personnel in the surgical resident staff, however, visiting surgeons find considerable difficulty in keeping the incoming men informed as to the complexities of the apparatus in use. It has, therefore, seemed to me to be of prime importance that the whole electrical armamentarium be simplified and standardized as much as possible. With the active cooperation and expert advice of the manufacturers, efforts have been made to simplify and make cheaper the apparatus necessary for satisfactory electrosurgery. The object has been to construct and standardize the apparatus so that perfect duplication of performance can always be depended on, and that no extraordinary electrical or mechanical aptitude is required of the surgeon; also to reduce the cost so that this great advance in surgery could be more universally adopted. I will not attempt to describe in detail the small compact machine to which the final model has been brought, as shown in Figure 1. The entire mechanism is encased in a wooden cabinet a little over one foot cube. There is only one adjustment, namely the lever which regulates the amount of power. The position of this lever shows one, at a glance, approximately how much output power it is set for. The spark gaps are fixed, and require no adjustment or attention. They will need compensation for wear about once every five hundred operations, and should have a useful life at least four times that great.[1] The entire gap assembly can be replaced in one unit at a minimal expense. A special arrangement maintains constantly accurate spacing of the spark gaps, irrespective of expansion and contraction of the metal due to temperature changes while in operation. This is very vital in obtaining uniform reproducible results.

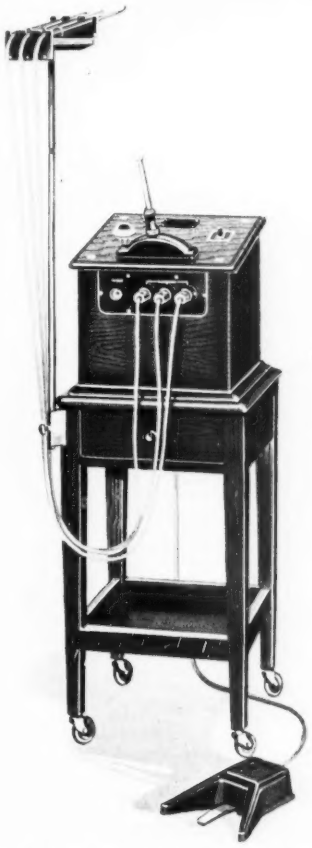

Fig. 1. High frequency electric apparatus or "coagulator" designed by Liebel Flarsheim in conjunction with the author.

A very important feature is that all of the voltage of the electric circuit is developed in one direction. In other words, the terminal marked "patient" is substantially at earth potential, so that the surgeon can touch any portion of the patient without danger of the high frequency current backing up and puncturing his glove or burning his fingers. The electrical circuits are completely ground free, and therefore shockproof. The patient need not be especially insulated from any metal objects, although where the patient does come in contact with the metal, this contact should be a good one to prevent sparking or

[1] Much of these details have been furnished by the Liebel Flarsheim Company, Cincinnati, Ohio.

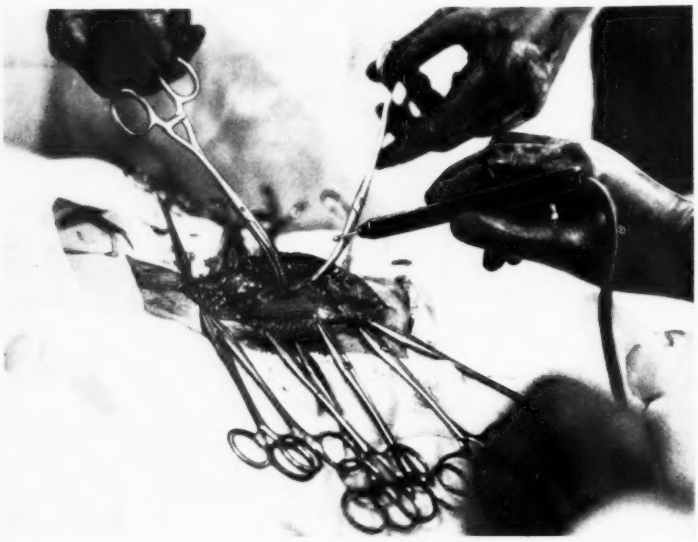

Fig. 2. Showing method of applying electrode momentarily to arrest bleeding point.

burns from a slight amount of "static" always present when high frequency apparatus is in use. A new device, by which the lever controlling the amount of current is locked in place, so that it cannot be moved by the accidental touch of an assistant during the operation, is an important feature. Into this lever a glass rod can be inserted and locked. It is sterilized with the instruments, and put in place at the beginning of the operation. The cords, electrodes and their holder are also sterilizable, and when not in use are held in the sterilizable rack, as shown in Figure 1. In order that the operator may have at hand several different types of electrodes ready for instant use, three such cords with operating handles are provided in addition to the cord which is attached to the metal plate upon which the patient lies.

When the surgeon has determined exactly the amount of current required for the type of work he is going to do, it is only necessary to set the lever at this point on the numbered scale in order to have exactly the same current at each operation. The length of time for each application of the electrode, of course, will vary according to the situation, and that alone will come with surgical experience. The object of the surgeon should be to use no more current than necessary, and for as short a period as will accomplish what he wishes. I found the apparatus most valuable in replacing ligatures for the arrest of hæmorrhage from bleeding points that have been clamped during operation. When it is desired to remove these clamps, the operator and staff can carry out an extremely rapid technique in which the assistants have the clamps elevated in position, and the operator touches only momentarily each clamp (Fig. 2), which is then removed by the assistants. In this way some fifty clamps can often be removed in a minute. The electrical current hardly does more than to cause a sealing of the bleeding points and very little destruction of tissue or actual necrosis. In cases in which the mass of tissue is larger and in which the mass contains vessels of distinct size, a little longer contact of the electrode upon the shaft of the clamp is necessary, but here again the operator should aim to avoid any more tissue injury than is absolutely necessary. If arteries or veins of importance are encountered, they should usually be marked for ligaturing with catgut or silk, but even in these cases with care it is often possible with the electrode to obtain hæmostasis and satisfactory sealing of the vessel. The use of the electrical current in such cases will have to be guided by the experience and prudence of the surgeon. In important operations it is wise not to take any chances lest this important advance in surgery be discredited.

Electrosurgery has apparently revolutionized hæmostasis in brain surgery and is one of the greatest advances in modern neurosurgery. In

operations upon the cortex of the kidney, we have long used some form of electrosurgery to avoid great hæmorrhage. The ordinary electrocautery has for this purpose been valuable, but the use of electrocoagulation by the high frequency current is still more valuable, and G. Ward deserves much credit for his demonstration of the great value of both the electric scalpel and the high frequency snare in removing portions of the kidney (and also spleen and liver) and in the avoidance of hæmorrhage. The only objection to the more considerable electrical current which is necessary to carry out such procedures is that tissue coagulation extends more deeply than in the trivial destruction necessary for cessation of hæmorrhage by the light application of the current to clamped areas, but as Ward has shown, even though such areas are not approximated by sutures, healing of the kidney wound is satisfactory. Further experience may be necessary to determine whether it is safe to do away completely with ligatures of the important vessels in the renal tissues, which have been arrested by the electrical snare or knife. I have found this apparatus particularly adapted to the fulguration or electrocoagulation of vesical tumors by means of the cystoscope or suprapubically. The manufacturers have, I believe, obtained in a marked degree the desiderata of simplicity, completeness, transportability, and marked reduction in price, everything which they were asked to accomplish.

THE RELATION OF DIVERTICULA OF THE BLADDER TO OBSTRUCTION OF THE VESICAL NECK

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IMPROVEMENT in methods of urologic diagnosis has made the finding of diverticula of the bladder far more simple than formerly when they were found only at necropsy or accidentally at the time of operation on the bladder. It was not until 1906 that Young added 3 cases to the 5 that had been reported in which diverticula had been successfully excised. Now, with recognition of obstruction of the vesical neck, infection within the bladder, and due regard to renal function, surgical treatment has become fairly common.

Diverticula of the bladder occur with all types of obstruction of the vesical neck, but not all cases of obstruction are associated with diverticula. Why this is so, and why good results are obtained in certain cases and in others the patients must almost continually be under the watchful eye of their physician remains to be determined.

Fig. 1. Extravesical excision of diverticulum of the bladder.

REVIEW OF MATERIAL

In the 30 cases chosen for this review, operation had been performed by one of us (Walters) in the course of the last 3 years. All of the cases have been studied in detail. A few were chosen for presentation because of some marked feature of interest in the observations, operation, or end-results.

Age. Sixty years was the average age of the patients. Five patients were aged less than 44 years, 4 of whom were in the fourth decade of life; in these 5 cases there were several features in common. The ages were 34, 37, 38, 38, and 43 years, respectively. The youngest had the shortest history, that of trauma to the perineum 4 months previously, with later retention of urine. The next older had sudden complete retention from urethral stricture and could not be catheterized. One of the patients aged 38 years had had flakes and pus in the urine for years. The other patient who was aged 38 years, and the patient who was aged 43 years had had difficulty in emptying the bladder for 18 and 20 years, respectively; the latter noted burning on urination at the age of 6 years. Therefore, young adults with diverticula had had obstruction at the vesical neck of long standing, or obstruction of the urethra had occurred from trauma.

Symptoms. The complaint of all the patients was urinary obstruction. The average duration of the complaints was 8.7 years, indicating that the process, as a rule, was rather prolonged. More than half of the patients complained of nocturia and frequency as the most prominent symptoms. In an equal number there was difficulty in urination, such as slowness in starting the stream, and a feeling that the bladder was not empty. Painful urination and burning were usually late symptoms and were accompanied by pain in the bladder and in the perineum. Hæmaturia was uncommon, whereas cloudy urine was noted by the patient in about a third of the cases.

Observations at examination. A high degree of infection of the urine was noted in all but 4 of the cases.

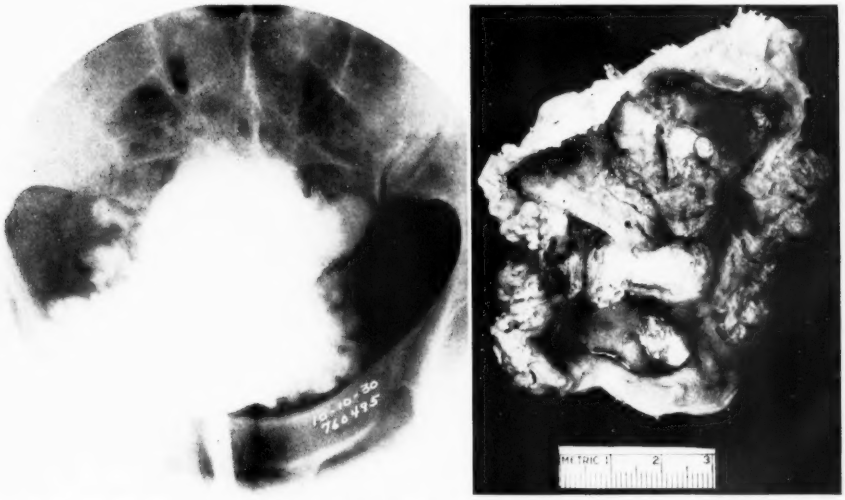

Fig. 2. At left, diverticulum in region of left side of dome of bladder. Both bladder and diverticulum filled with opaque solution; at right, diverticulum resected, disclosing stones.

Even though it seemed that the diverticula were associated with prolonged obstruction at the neck of the bladder, the phenolsulphonephthalein test indicated good renal function, as a rule; in most cases 40 to 50 per cent of the dye was excreted in 2 hours. In cases in which renal function was not good, suprapubic drainage seemed to restore satisfactory ability to excrete the dye. This indicated that renal injury probably was not permanent. Other tests of renal function, such as determination of blood urea, were parallel.

The quantity of residual urine in the bladder was large; 12 ounces (350 cubic centimeters) was the average. In only one case was residual urine absent. In 10 cases the bladder was so distended as to extend above the symphysis pubis.

Cystoscopy and cystography. The cystoscope or the cystogram was used in all of these cases, and thus, accurate knowledge of the condition within the bladder was known before operation. Since the cystogram has become common in the visualization of the bladder, the accidental finding of diverticula at operation is almost unknown. By combining the use of the cystoscope and the cystogram, the surgeon can outline his course of attack before the bladder has been opened.

Associated lesions. Because we believe that diverticula are caused by congenital weakness of the bladder that is manifested because of the obstruction, a study was made to see how much evidence of other abnormalities could be found. The result was unexpected. Almost half of the patients had hernias of some sort, that had been present all their lives or had developed following some other operation or injury. The hernias were, in the order of frequency, inguinal, ventral, umbilical, femoral, and diaphragmatic. Obesity was marked in about a third of the cases. Diabetes was found in 3 cases and unilateral complete du-

Fig. 3. Large diverticulum arising from right wall.

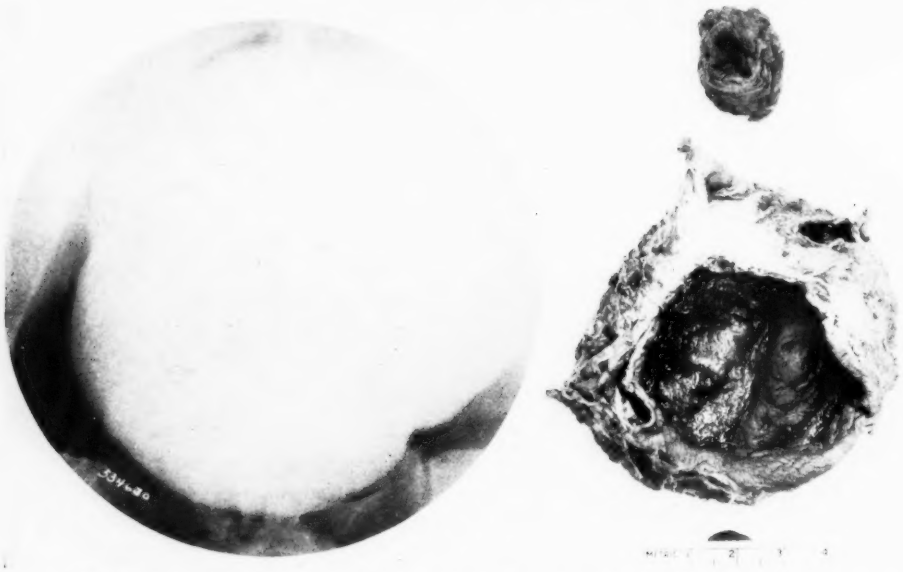

Fig. 4. At left, large diverticulum equal to bladder in size; at right, two diverticula resected.

plication of the renal pelvis and of the ureter was found in 1 case. The great number of hernias present makes it appear that congenital weakness of the tissues has something to do with the development of diverticula, and that congenital anomalies may account for a smaller number. Multiple diverticula were found in 7 cases.

Types of obstruction at the vesical neck. Diverticula of the bladder in adults practically always are seen in the presence of obstruction at the vesical neck. This no doubt accounts for the fact that a very large proportion of the patients with diverticula are men. All of our patients were males. Judd, in 1924, reported a series of 133 cases, only two of which affected women. Thus, it appears that weakness of the musculature of the bladder, either due to congenital defect or anomaly, together with the mechanical factor of obstruction, is the first cause of diverticula.

In more than half of our cases (17), definite fibro-adenomatous hypertrophy of the prostate gland made prostatectomy advisable as may be noted in Cases 4 and 5. However, the smaller the prostate gland appeared to be at operation, the longer the symptoms seemed to have been present.

A definite median bar (Cases 1 and 6), formed of the substance of the prostate gland itself, or by inflammatory tissue, was noted in 5 cases.

Cicatricial contraction of the vesical neck may occur (Case 3), and can be remedied by a plastic procedure on the vesical neck at the time of diverticulectomy, by a subsequent punch operation, or by incision with the Collings knife. There were 4 such cases in this series.

In cases in which there is a long history of difficulty, and there is no evidence of prostatic hypertrophy or of a median bar, a chronic cicatricial posterior urethritis with obstruction of the vesical neck may be present (Case 2). In these cases excision or dilatation of the urethral structure is necessary for relief of symptoms. Four of our cases fell into this group.

OPERATIVE PROCEDURES

Excision of the diverticulum is the only operation which gives uniformly good results. The pouch-like structure, depending on its size, its accessibility, or its situation, can be excised by one of three methods: (1) extravesical, (2) transvesical, or (3) intravesical. The operation that can be applied divides the cases into three groups.

EXTRAVESICAL EXCISION AND ILLUSTRATIVE CASES

Extravesical excision (Fig. 1) is usually applied to large diverticula that can be separated from the surrounding structures by careful dissection. It was employed in 19 of our cases.

The bladder is incised, and the opening or neck of the diverticulum is found. The surrounding

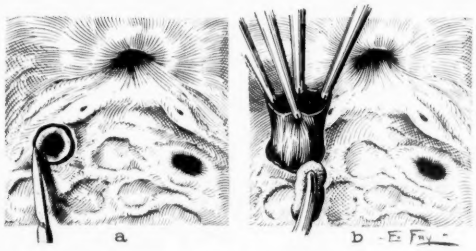

Fig. 5. At left, circular incision around neck of diverticulum; at right, transvesical dissection of sac of diverticulum.

tissues are then thoroughly protected with gauze packs. The pus and urine are swabbed out of the pouch. The diverticulum is thoroughly cleansed from within with 2.5 per cent aqueous solution of mercurochrome.

Many ingenious methods have been devised for holding the diverticulum open during dissection. Lerche suggested the method of inflating a small rubber bag, after inserting it into the diverticulum. Lower suggested packing the diverticulum full of gauze, so that it may be well outlined, or traction may be exerted by fingers inserted into the sac, and the dissection can be made by bimanual manipulation. Large diverticula are almost always adherent to the ureter. A ureteral catheter inserted into the ureter will assist in identification and aid in avoiding injury.

The diverticulum is dissected free from surrounding tissues and is excised at the neck. The vesical mucous membrane is then closed by sutures over which the vesical muscle is approximated by two rows of interrupted sutures of chromic catgut. The ureteral catheter can then be removed. It is usually advisable to place a drain in the perivesical space at the point where the sac was dissected free. The bladder is then temporarily drained by means of a catheter carried out the suprapubic incision.

Case 1. A man, aged 56 years, had a huge, multiloculated diverticulum which contained many stones. He gave a long history of obstruction of the vesical neck due to a median bar. A stone had been removed from the bladder in 1920 after 4 years of difficulty. For 6 years he had had frequency, and burning on urination. In the 6 to 9 months before his registration, he had experienced difficulty in starting the stream and had lost 25 pounds. The bladder was distended upward as high as the umbilicus. The concentration of urea in the blood was 62 milligrams in each 100 cubic centimeters; roentgenograms of the region of the bladder gave evidence of multiple vesical calculi; a cystogram (Fig. 2) disclosed a large diverticulum 6 by 4 centimeters in various diameters, arising from the dome.

At operation, October 10, 1930, a huge diverticulum (Fig. 2) 7.5 and 5 centimeters in various diameters was found lying on top of, and mesial to, the left ureter. The diverticulum, which contained two stones, was removed by the extravesical method. The patient gained 15 pounds in weight in 18 days but there was difficulty in getting the wound to heal. A transuretheral punch operation was performed November 5, a fibrous median bar being removed. There did not seem to be any fibro-adenomatous hypertrophy of the prostate gland.

Fig. 6. Diverticula arising from right and left sides of bladder. The bladder is empty.

Case 2. A man, aged 38 years, had been troubled by straining on urination for 15 or 20 years. He had a feeling that the bladder did not empty. Dilatation of a urethral stricture had given some relief. There was cystographic evidence of a diverticulum, arising from the right wall of the bladder, equal in size to the bladder (Fig. 3). Chronic cicatricial urethritis was present, and there were 9 ounces (270 cubic centimeters) of residual urine.

At operation, September 23, 1930, a diverticulum, 7.5 centimeters in diameter, arising from the right wall of the bladder about 1.5 centimeters from the right ureteral orifice, was removed by extravesical excision. The postoperative course was normal for 21 days and the suprapubic wound was dry. On the twenty-second day there were chills and fever, which disappeared following drainage of the bladder by means of a catheter. Removal of the urethral catheter was followed with urinary retention and return of chills and fever; the patient became weak and the value for urea in the blood mounted to 214 milligrams in each 100 cubic centimeters. Vomiting and gastric retention were noted on the fortieth day after operation. The suprapubic tube was replaced; fluids were given by vein twice a day; gastric lavage was carried out twice a day, and the value for blood urea returned to normal in 2 weeks.

The patient was sent home on the sixtieth day after operation, wearing a suprapubic tube, to return for operation on the vesical neck later. He was seen 2 months later; then his weight was returning to normal and he felt better, but the value for blood urea was still elevated to 76 milligrams in each 100 cubic centimeters. Operation was deferred.

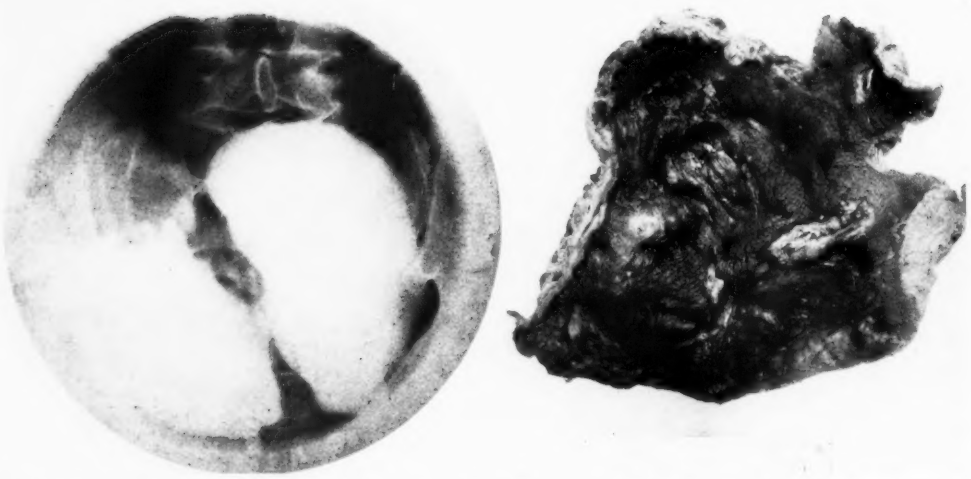

Fig. 7 *a*. Huge diverticulum on left wall of bladder, and smaller one on right; *b*, diverticulum resected; it was equal to the bladder in size.

CASE 3. A man, aged 48 years, had noticed increasing frequency and nocturia for 3 years before his registration at the clinic. He also had difficulty in starting the urinary stream, straining on urination, and cloudy urine. Pus in urine was graded 3. The bladder was huge, and the cystogram (Fig. 4) gave evidence of a diverticulum high in the median line, 6 and 8 centimeters in various diameters, when the bladder was empty, and apparently twice that size when it was distended. There was evidence of chronic prostatitis and there were 14 ounces (420 cubic centimeters) of residual urine.

January 6, 1926, two diverticula of the bladder were found at operation (Fig. 4). The larger lay posterior to the bladder, and opened just posterior to the left ureteral orifice. This diverticulum had a capacity of about 6 ounces (180 cubic centimeters). The smaller diverticulum had a capacity of 1.5 ounces (45 cubic centimeters) and was situated on the left lateral wall, with its opening about 5 centimeters lateral to the larger one. Both diverticula were removed by extravesical excision.

Convalescence was uneventful and the patient was dismissed from hospital on the twenty-eighth day after operation. The suprapubic sinus was healed at that time. Two weeks later, chills and fever appeared and 5 to 6.5 ounces (150 to 200 cubic centimeters) of residual urine was obtained. A punch operation was performed March 9, 1926, for contraction of the vesical neck. Two months later, the patient said that his health was excellent. One and a half years later, he said that the urinary stream was of good volume and that it started without difficulty.

TRANSVESICAL EXCISION AND ILLUSTRATIVE CASES

If there is evidence of marked perivesical inflammation, if the bladder has been previously drained and much scar tissue is present, making extravesical dissection difficult and hazardous because of the possibility of opening the peritoneal cavity, and if the diverticulum is not too large, the transvesical method suggested by Geraghty is indicated. This type of procedure was applied in 5 of our cases.

The wall of the diverticulum is made up of two main layers. These are the mucosa, and an outer, fibrous layer, between which there are sometimes a few muscle fibers. The bladder is opened suprapubically as in the former method and good exposure of the diverticulum is obtained. A circular incision (Fig. 5) is then made around the neck of the diverticulum, through the bladder. The fibrous ring can be incised in either direction in order to facilitate manipulation in dissection. The entire diverticulum is removed by a process of sharp, combined with blunt, dissection (Fig. 5). The muscles of the wall of the bladder are brought together by interrupted sutures of chromic catgut, and the mucosa is sutured over this with plain catgut. A Penrose drain may be placed temporarily to the outer side of the bladder, and a No. 30 catheter is placed in the bladder for suprapubic drainage, and is left in place until further operation on the neck of the bladder is done to relieve any existing obstruction.

CASE 4. A man, aged 70 years, had had increasing frequency and nocturia for 2 or 3 years. He felt that the bladder did not empty, and he had noted cloudy urine. On examination, arteriosclerosis was graded 2; the prostate gland was palpated by rectum and was enlarged (graded 2). The amount of pus in the urine was graded 2. A cystogram (Fig. 6) gave evidence of a hugely dilated bladder, with diverticula on either side, of several ounces capacity, which

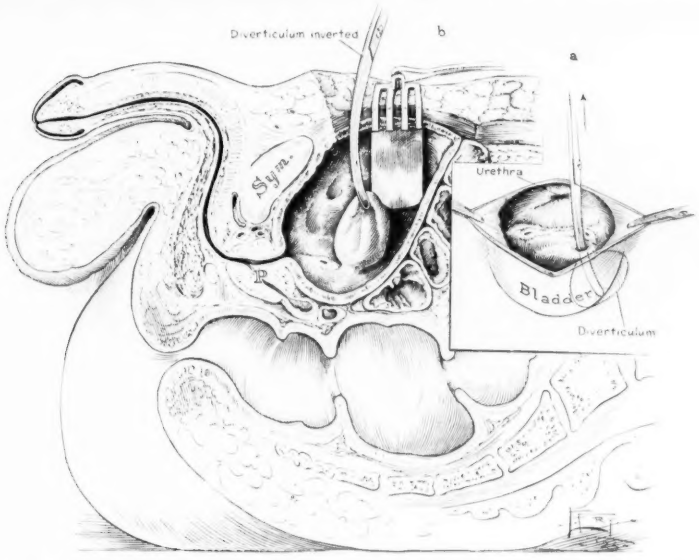

Fig. 8. Intravesical removal of diverticulum of bladder. Insert shows method of grasping the fundus of diverticulum preparatory to inverting it into bladder.

did not empty. There was a stone in the diverticulum on the right side, and residual urine measured 3 ounces (90 cubic centimeters).

At operation, April 21, 1926, two small diverticula were noted at the base of the bladder. The right one contained a stone about 3 centimeters in diameter, which was removed. There was much pus in each diverticulum. The necks of the diverticula were widened and the bladder was drained. At a second operation, May 24, 1926, the diverticula were removed by an approach from within the bladder. Transvesical dissection was done and the bladder was again drained. June 16, 1926, at a third operation, suprapubic enucleation of the prostate gland was carried out. Chronic prostatitis and some adenofibromatous hypertrophy were present. The bladder was found to be clean at this operation.

Convalescence was uneventful. In a letter, received 4½ years afterward, the patient stated, "I am feeling fine and am working every day. There is no burning or frequency of urination."

This case illustrates the excellent results of diverticulectomy, with secondary removal of an obstructing prostate gland.

CASE 5. A man, aged 66 years, had had frequency, burning, nocturia, and a slow stream for 15 years. He had had acute retention 12 years before his registration at the clinic. Arteriosclerosis was graded 3. Vesical dullness extended to the umbilicus, and there was 1,500 cubic centimeters of residual urine. A left inguinal hernia, and a small umbilical hernia were present. The proportion of erythrocytes in the urine was graded 3, and pus 2. Cystoscopic examination revealed cystitis of high grade, with many granulations. A diverticulum, of greater capacity than the bladder, arose from the left portion of its base.

May 23, 1928, the diverticulum, which was approximately 15 centimeters in diameter (Fig. 7), was removed by extravesical dissection. A smaller diverticulum was noted on the right wall. The bladder was drained. June 13 this smaller diverticulum (7.5 centimeters in diameter) was resected by transvesical excision. The adenofibromatous prostate gland was enucleated at this time.

The wound healed with difficulty. Marked cystitis was treated by lavage and catheterization three times a day. A letter, received 2½ years later, contained the information that the patient was in good health, that he was passing a normal stream, and that he had no symptoms.

INTRAVESICAL EXCISION AND ILLUSTRATIVE CASE

This method, described by Young in 1906, like the one just mentioned, has its virtue in that the mucous membrane can be made to separate from the wall of the sac rather easily in some cases. The procedure is usually applicable to treatment of rather small diverticula. In cases in which infection is present around the sac, resort must be had to one of the two former methods.

The bladder is opened suprapubically and the orifice of the diverticulum is exposed. A pair of forceps is passed into the orifice of the diverticulum and the fundus is firmly grasped. Traction with the forceps is made toward the interior of the bladder and the sac is inverted (Fig. 8) into the bladder. The sac is then cut off at the neck. The muscles are closed by interrupted sutures. The mucosa is then brought together over

Fig. 9. Small diverticulum of left wall of bladder.

this row of sutures. A drainage tube for urine is placed in the bladder and the bladder is closed around it. Diverticula were removed by this method in 4 cases.

CASE 6. A man, aged 37 years, was found to have a marked pyuria. He had bilateral inguinal hernias; erythrocytes in the urine were graded 1, and pus 4. A cystogram (Fig. 9) gave evidence of a smooth diverticulum of the left wall of the bladder. On cystoscopic examination this diverticulum appeared to be 2 by 2.5 centimeters. Chronic prostatitis was present, and there was a bar, graded 2, at the neck of the bladder.

October 10, 1930, the diverticulum was pulled into the bladder (inverted) and excised; the median bar and posterior lobe of the prostate gland were removed. The suprapubic tube was removed on the tenth day. The wound healed readily. October 28, 1930, bilateral herniorrhaphy was performed.

November 18 the patient was dismissed from observation. At that time, the urine was clear, and the patient was feeling well.

RESULTS

In more than two-thirds of the cases in which the diverticulum was removed the results were good. In 2 cases the results were fair; the patients were relieved of most of the troublesome symptoms. Five patients continue to complain of dysuria. The latter group consisted of the case in which the vesical necks were the site of inflammatory cicatricial change, with or without accompanying posterior urethritis. Removal of a portion of this sclerosed vesical neck by the punch operation did not always serve immediately to relieve the urinary retention, possibly because of the surrounding inflammatory tissue and possibly because there may have been some fundamental abnormality of neuromuscular control of the bladder. This group included most of the younger men.

The best results occurred in those cases in which the obstruction at the vesical neck was thoroughly removed, either at the time of diverticulectomy, or subsequently. In other words, patients with associated hypertrophy of the prostate gland, who underwent prostatectomy, obtained the best results. Similar results occurred in most cases in which a punch operation for obstructing median bar was performed.

CONCLUSIONS

Diverticula of the bladder are being found with increasing frequency. Surgical treatment consists of their removal. Successful relief of symptoms after diverticulectomy is dependent on the completeness of removal of obstruction at the vesical neck.

BIBLIOGRAPHY

1. GERAGHTY, J. T. A simple procedure for the radical cure of large vesical diverticula. South. M. J., 1922, xv, 54-57.
2. HINMAN, FRANK. The etiology of vesical diverticulum. J. Urol., 1919, iii, 207–246.
3. HUNT, V. C. Surgery of the lower urinary tract. Illinois M. J., 1925, xlvii, 222–227.
4. JUDD, E. S. Diverticula of the bladder. Ann. Surg., 1918, lxviii, 298–305.
5. LERCHE, WILLIAM. The surgical treatment of diverticulum of the urinary bladder; with the report of a case and a new device for facilitating the operation. J.-Lancet, 1912, xxxii, 337–342.
6. LOWER, W. E. An improved method of removing a diverticulum of the urinary bladder. Cleveland M. J., 1914, xiii, 1–7.
7. WALTERS, WALTMAN, and MULHOLLAND, S. W. Diverticulum of the bladder; report of six cases. Proc. Staff Meetings of Mayo Clinic, 1930, v, 347–349.
8. YOUNG, H. H. The operative treatment of vesical diverticula with report of four cases. Johns Hopkins Hosp. Rep., 1906, xiii, 411–446.

PRIMARY MALIGNANT NEOPLASMS OF THE EPIDIDYMIS

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MALIGNANT tumors of the testicle are rare. According to Keller, who made a study of 28 cases in the Municipal Hospital at Copenhagen, they occur once in 15,000 cases. Apparently they are somewhat more numerous in America because in 300,000 cases admitted to the Mayo Clinic, 50 cases of neoplasm of the testicle were found (22). Primary malignancy of the epididymis is of even less frequent occurrence. In the literature we have been able to find reports of only 21 instances of malignant neoplasm which were considered to be primary in the epididymis. In view of this fact, we wish to present the clinical and pathological findings in a case of primary malignant teratoma of the epididymis.

Mr. F. H., aged 51 years, came to us on August 5, 1928, because of a swelling in the right side of the scrotum. A few days previously he had experienced a sense of heaviness in the right half of the scrotum and he stated that the right testicle seemed to be somewhat enlarged and slightly tender. He had never suffered any acute pain in that region, but the mental annoyance caused him to seek relief. He had no recollection of any injury to the scrotum. There were no symptoms referable to the gastro-intestinal, cardio-respiratory, or nervous systems. The family history was negative for tuberculosis, cancer, and syphilis.

The general physical examination showed no essential abnormalities.

The urological examination revealed a slightly enlarged right epididymis, of hard nodular consistence and moderately tender to pressure. The right testicle appeared to be normal in size, shape, and consistence. There was no fluid in the tunica vaginalis propria. The left testicle and epididymis were normal. Rectal examination showed the prostate gland to be slightly enlarged, freely movable, and smooth; the median commissure was almost obliterated. The expressed prostatic secretion contained only an occasional pus cell. There was no urethral discharge.

The urine showed a very faint trace of albumin, an occasional hyaline cast, and a few scattered separate pus cells. Numerous stained smears and animal inoculations failed to reveal the presence of tubercle bacilli. X-ray studies of the chest showed no evidence of active tuberculosis or metastatic neoplasm. The blood Wassermann and Kahn reactions were negative.

A tentative diagnosis of tuberculous epididymitis was made. The patient was admitted to the Miami Valley Hospital on August 25, 1928, at which time the operation was performed.

A longitudinal incision, 7 centimeters in length, was made on the anterior portion of the right side of the scrotum. The right testicle and epididymis were delivered into the wound. There were no scrotal adhesions. The body of the epididymis was slightly enlarged, rather hard, and definitely nodular. The globus major of the epididymis was not involved. The testicle was smooth and of normal size and consistence. The epididymis was easily separated from the testicle by passing a blunt hæmostat between them. The epididymis was removed from its testicular attachment by cautery. The vas deferens was ligated at the level of the external inguinal ring. The scrotal fascia was closed by No. 0 chromic catgut and the skin edges were approximated with metal skin clips.

Pathological examination. The microscopic examination of sections taken from the firm yellowish-white mass, measuring 5 by 3 by 2 centimeters, revealed a diffusely infiltrating neoplasm, in which the predominating cell type was a large, round, or spindle-shaped cell with pale, clear cytoplasm and a large, hyperchromatic nucleus. Scattered here and there were small deeply staining round cells of the lymphocytic type. The tubules of the epididymis were widely separated by the neoplasm cells. The histopathological diagnosis was malignant teratoma, composed of highly undifferentiated embryonal cells; this neoplasm possessed the histological characteristics of the so called embryonal carcinoma with lymphoid stroma. This teratomatous new-growth was structurally identical with the most common form of malignant neoplasm originating in the testis.

Sections were submitted to Aldred Scott Warthin, professor of pathology at the University of Michigan. Doctor Warthin's diagnosis was: "Malignant teratoma, of the undifferentiated embryonal carcinoma type."

The patient was informed of the pathological diagnosis and a more radical operation was proposed but he refused to submit to any further treatment.

The postoperative convalescence was uneventful. The skin clips were removed on the seventh day and the patient was dismissed from the hospital on the tenth day following the operation.

Nothing more was heard of the patient until May 27, 1929, when he presented himself to Doctor E. R. Arn for a vague gastro-intestinal complaint and the loss of 15 pounds in weight. Examination at this time revealed a small grapefruit size, firm, nodular mass in the right upper abdominal quadrant. Because of the previous history, Doctor Arn made a diagnosis of metastatic malignancy of the retroperitoneal lymph nodes.

The general condition of the patient contined to pursue a downward course until the time of his death on July 6, 1929, about 10 months after the operation.

The pertinent findings at the postmortem examination follow:

The body was that of an undernourished, emaciated, senile appearing white adult male, looking much older than the stated age. The external examination revealed little of importance, except the presence of a completely healed linear scar 1 inch in length in the scrotum overlying the right epididymis. The spinal cord and brain were not examined because of stated restrictions.

The heart showed no essential abnormalities. Both lungs contained localized areas of terminal lobular pneumonia; there were multiple scattered healed tubercles. The bronchial lymph nodes contained many healed calcified tubercles.

The abdomen contained a large, firm, whitish retroperitoneal tumor mass which extended from the brim of the true pelvis to the inferior surface of the liver. The mass

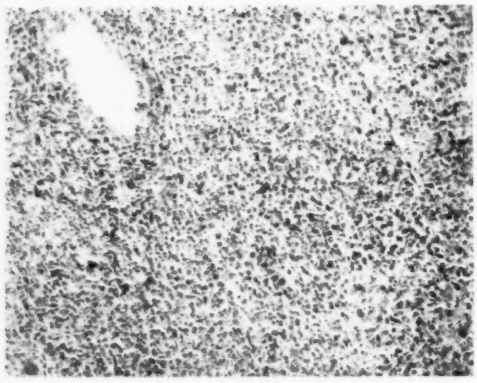

Fig. 1. Photomicrograph of primary embryonal carcinoma of right epididymis, showing tubule of epididymis in upper left quadrant of photomicrograph. The neoplasm cells, showing pale clear cytoplasm and large hyperchromatic nuclei are seen, together with the characteristic lymphoid stroma.

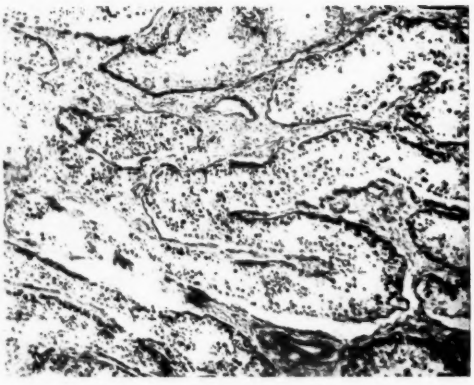

Fig. 2. Photomicrograph of tissue from right testicle, adjacent to site of the primary neoplasm of the epididymis, showing atrophy and vacuolization of the germinal epithelium with aspermatogenesis. There is no evidence of testicular neoplasm.

was made up of enormously enlarged retroperitoneal lymph nodes. Completely surrounded by the mass were the right kidney and adrenal, the head of the pancreas and the abdominal aorta. Just below the head of the pancreas, the mass assumed the size of a large grapefruit (15 by 12 by 10 centimeters). The liver showed fatty infiltration, marked cloudy swelling and congestion, but no evidence of neoplasm. The neoplastic mass surrounding the right kidney had extended to, but not through, the fibrous capsule. The kidneys showed marked cloudy swelling but no evidence of neoplasm. The right ureter was partially obstructed by the neoplastic mass with the result that the renal pelvis was dilated to about twice the normal size. The aorta showed slight atherosclerosis; there was no evidence of syphilitic aortitis.

There were no penile scars. The right testicle was bound to the healed surgical incision by many adhesions. There was no gross evidence of neoplasm of either epididymis or either testicle. The prostate gland was about one and one-half times normal size and showed localized pea-size areas of glandular hyperplasia on either side of the prostatic urethra.

Microscopic examination of tissue from the greatly enlarged retroperitoneal lymph nodes showed the same type of neoplasm as was found in the mass removed from the right epididymis 9 months previously. There was no microscopic evidence of neoplastic invasion of the parenchyma of the right kidney, right adrenal, and body of the pancreas.

Serial sections of the remaining portion of the right epididymis showed no evidence of recurrence of the neoplasm. The testicles showed atrophy and vacuolization of the germinal epithelium with aspermatogenesis. The tunica albuginea of the right testicle showed no neoplastic infiltration.

Microscopic studies of lung tissue showed localized areas of acute terminal lobular pneumonia with small localized areas of completely healed fibroid tuberculosis.

The pathological diagnosis was: Advanced retroperitoneal metastatic carcinomatosis, involving all of the retroperitoneal lymph nodes, with direct extension of the neoplasm to the capsules of the right kidney and right adrenal, right ureter, head of pancreas, and abdominal aorta. (Primary malignant teratoma, embryonal carcinoma type, removed surgically 9 months previously.) Right obstructive hydronephrosis. Acute terminal bilateral purulent lobular pneumonia. Healed pulmonary and bronchial node tuberculosis. Early atherosclerosis. Passive congestion and cloudy swelling of all organs. Cachexia.

The essential features of this case are concerned with the development of a primary malignant teratoma in the right epididymis. The neoplasm was of the type generally considered to be an undifferentiated embryonal carcinoma. This type of neoplasm commonly originates in the testicle. The postmortem examination revealed no evidence of testicular origin of the neoplasm in this case.

PREVIOUSLY REPORTED CASES

A review of the world's literature reveals that only 21 authentic cases of primary malignancy of the epididymis have been reported. Abstracts of the previously reported cases follow:

CASE 1. Lente and Jacobus reported the pathological examination of a specimen. No clinical history was given. The epididymis was destroyed or replaced by a new-growth which, on section, showed numerous small cysts filled with a thick yellowish matter and clusters of hyaline cartilage. The cysts were lined with tessellated epithelium. The semisolid matter was composed of medium sized, rounded corpuscles imbedded in a homogeneous matrix. The testicle was normal except for degeneration of the epithelial elements.

CASE 2. Edwards reports the case of a man aged 50 years whose general health had always been excellent until 18 months previously when he developed gonorrhœa. One year later he had rheumatism. Six weeks before admission he noticed a pea-size nodule just above the left testicle.

This increased in size and became painful and when first seen by the surgeon had reached the proportions of a walnut in the region of the globus major and was accompanied by a smaller tumor in the globus minor. The testicle and both masses were tender. Biopsy revealed the tumor to be round cell sarcoma. Castration was done. A new-growth the size of a marble attached to the posterior surface of the globus major was removed. The vas deferens was also infiltrated. Microscopically, there was an infiltration with small round cells. In places these appeared to be undergoing organization but a combination of the clinical and histological characteristics appeared to favor malignancy.

CASE 3. Kocher and Langhans. A man aged 50 years was operated upon 3 weeks after he first noticed an enlargement of the scrotum associated with drawing pains. At this time a hard, firm epididymis could be palpated behind a normal testicle. Two months after the initial operation, castration was done. Soon after this, he developed metastasis to the nerve centers and later to the skin and lungs. Death occured shortly after the appearance of metastatic lesions. The diagnosis was primary sarcoma of the tail of the epididymis.

CASE 4. Kocher and Langhans describe a case of melanosarcoma originating in the tail of the epididymis. This growth later invaded the testicle. No further history was given.

CASE 5. Kocher and Langhans report a case of cystosarcoma of the epididymis. This consisted of a very thick walled cyst in which the epididymal canals could be seen between the new formations of round cells. The testicle rested on the mass but was macroscopically normal. No further history was given.

CASE 6. Rydygier. A 42 year old physician noticed a pea-size swelling in the epididymis. As this was associated with drawing pains in the pelvis he demanded a castration. This was immediately done. The swelling was found to have arisen from the head of the epididymis. The growth measured 1.5 by 1 centimeter. Microscopically it showed the characteristics of a typical melanosarcoma. The cells were spindle shaped and were in some places filled with a black brown pigment. The epithelium of some of the seminal ducts was invaded while many others remained normal. Four weeks after the operation the patient returned and demanded the removal of the remaining testicle because he felt a nodule there. This operation was done and the pathologist reported a brownish pigmentation of the epithelial cells of the epididymis. However, this epididymis apparently was not sarcomatous.

CASE 7. Bazy (2). A man aged 48 years had noticed some enlargement of one of his testicles ever since the development of gonorrhœal epididymitis 25 years previously. Two months before admission he received an injury to the testicle and after that time it increased rather rapidly in size. On admission it was the size of a goose egg, pear shaped, and of firm consistence except in one spot where there was fluctuation. Anti-luetic treatment caused no improvement. The glands of the abdomen were not enlarged. The testicle and epididymis were removed, and the body of Highmore and the epididymis were found to be the seat of a small round cell sarcoma. The remainder of the testicle was normal. A subsequent report (3) states that the growth probably arose in the rete testis and from there invaded the epididymis but not the testicle.

CASE 8. Kolster. A farmer 52 years of age came to the clinic because of dyspnœa. A diagnosis of malignant tumor of the mediastinum was made. The autopsy showed a round cell sarcoma of the epididymis with metastasis to the lymph nodes of the left inguinal region, the nodes along the left side of the spine, the left lung, the liver, and the cardiac end of the stomach. One mass in the left lumbar region was as large as a child's head and another mass in the mediastinum passed up under the left sternomastoid muscle into the left supraclavicular fossa where it reached the size of a goose egg. The left testicle was entirely normal. The primary growth and the metastatic nodules all showed the structure of a round cell sarcoma.

CASE 9. Russell and Wood. A boy aged 15 had had three definite injuries to the left testicle. When first seen he had a boat-shaped tumor about 4 inches in length in the region of the left testicle. About 1 week later a nodule appeared in the upper portion of the growth and fluctuation was noticed. Two days later the tumor was removed. It was kidney shaped and weighed three-fourths of a pound. The testicle was located behind the mass and was found to be normal. Microscopic sections showed the new-growth to be composed of large and small round cells and spindle cells. The connective tissue stroma was arranged in bundles and whorls.

CASE 10. Grasman. A man aged 42 years received a crushing injury to the left testicle 6 months prior to admission. Three months later he developed a swelling which gradually increased in size until it was as large as a man's fist. It was smooth, tense, elastic, and was associated with a small hydrocele. At operation a sarcoma of the epididymis was found. The testicle was normal except for the signs of compression. There was no recurrence 1 year later.

CASE 11. Wrobel reports the case of a man aged 24 years. Two years before admission he had arthritis complicated by heart trouble. Eighteen months later he experienced a recurrence of gonorrhœa. A short time before admission he noticed a swelling of the left testicle. This was accompanied by pricking pains. The epididymis and testicle contained nodules, some of which were as large as a hazelnut. The spermatic cord was similar'y involved. Castration was done and the microscopic examination showed carcinoma of the epididymis. Death occurred about 12 years later but the cause of death is not mentioned.

CASE 12. Miyata. A 32 year old man noticed a swelling of the left side of the scrotum 3 weeks before admission. The testicle was considerably enlarged, hard, and slightly tender. There was no swelling of the glands. The condition was diagnosed as chronic epididymitis and castration was performed. The pathological examination showed the testicle to be normal but there was a soft, juicy, encapsulated tumor about the size of a pear on the epididymis. The microscopic diagnosis was sarcoma.

CASE 13. Spandri. A man aged 80 years noticed a sense of heaviness in his right testicle about 1 year before admission. This disappeared under treatment but 11 months later he developed pain in his testicle, associated with swelling. When first seen, the scrotum was enormously enlarged. The tumor was smooth and of firm consistence, posteriorly. The tumor, spermatic cord, testicle, and epididymis were removed. The testicle was not involved. The epididymis was about three times normal size and was made up of a hard, compact elastic tissue, except in areas where it was opaque and of a yellowish color. Microscopically the form and arrangement of the cells, the abundant blood supply, the absence of epididymal tissue in these masses, and the presence of cartilage indicated that this growth was a chondrosarcoma.

CASE 14. Colby describes a case of columnar carcinoma of the epididymis occurring in a 32 year old man. When first seen the left globus major was slightly enlarged but distinct from the testicle. Six weeks later the globus major had increased in size and the globus minor was invaded but the testicle remained normal. The involvement in-

creased steadily and it became impossible to say which portion of the testicle was involved. At this stage the skin and the spermatic cord were involved. Castration was done and the specimen was found to be cystic. The microscopic examination showed columnar cell carcinoma. The patient was dismissed from the hospital and was not seen again for 9 months. At this time there was a mass about the size of a fetal head in the left hypochondrium. From this time he became steadily worse and death occurred 2 months later. Postmortem examination showed the abdomen to be filled with a single, smooth, elastic tumor which was cystic and friable and about the size of an association football. The origin could not be determined. Colby states that he believes carcinoma of the testicle frequently arises in the epididymis.

CASE 15. Rowlands and Nicholson. A 46 year old policeman suffered from a painful enlargement of the right testicle. This organ was always slightly larger than its mate, but following an injury 4 months before admission it gradually increased in size and became painful. At the time of admission there was moderate enlargement of the right side of the scrotum. Anteriorly, the swelling was smooth, soft, and translucent but posteriorly it was hard and somewhat irregular. In the latter position the enlarged epididymis could be felt. The testicle was not involved. There was slight thickening of the spermatic cord. Two weeks after admission the testicle, epididymis, and spermatic cord were removed. The wound healed by first intention. Nine days after operation œdema of the right leg was first noticed. The patient developed ascites and abdominal pain; death occurred about 7 weeks after operation. No autopsy was obtained. Microscopically the specimen obtained at operation revealed squamous cell carcinoma of the epididymis, tunica vaginalis, and a similar nodule in the spermatic cord.

CASE 16. Bland-Sutton. A man aged 31 first noticed enlargement of his testicle 8 months before admission. Since that time it gradually increased in size. The testicle, epididymis, vas deferens, and one lymph node were removed. The enlarged lymph node was situated in front of the vena cava on a level with the third lumbar vertebra. The tumor was found to be cystic and to occupy the space between the testicle and the epididymis. Microscopically the tumor was composed of intercommunicating tubules imbedded in a connective tissue stroma. In places hyaline cartilage was present and in other places tissue resembling unstriped muscle was found. The tubules were lined with epithelium some of which was stratified and some of which was columnar. The excised lymph node was cystic and was in some places lined by columnar epithelium. Bland-Sutton regarded this neoplasm as a malignant teratoma.

CASE 17. Sakaguchi. An 18 year old youth first noticed some swelling of the left testicle 14 weeks before operation. This swelling was associated with a varicocele. At the first operation the varicocele and as much as possible of the epididymis was removed. As the diagnosis was carcinoma a secondary castration was performed 3 days later. A short time after this the patient was dismissed from the hospital. He remained well until 9 months after the operation at which time he developed vague pulmonary symptoms. Definite metastasis was found and the patient gradually grew worse and died about 5 months after the onset of pulmonary symptoms. Autopsy showed extensive metastasis to both lungs and to the retroperitoneal and mediastinal lymph nodes.

Microscopic examination revealed carcinoma which the author considered to have arisen in the epithelium of the canals of the epididymis.

CASE 18. Barringer reports the case of a man who presented upon examination an enlargement of the right epididymis and a fairly large abdominal mass. The primary tumor was stony hard and somewhat irregular. At operation the spermatic cord was found to be thickened and one of its vessels ran into the abdominal mass. The tumor was treated by radium but the results are not given. The testicle and prostate were perfectly normal. The condition was diagnosed as teratoma of the epididymis.

CASE 19. LaPointe and Cain. A man, aged 66 years, had experienced pain in the left testicle for 2 years. Examination revealed a tumor of cherry seed size in the tail of the epididymis. This was slightly nodular and had the consistence of a slightly thickened cyst. At first this was thought to be the result of gonorrhœal epididymitis which he had 42 years previously, but, because of pain, castration was done. The tumor was made up of irregularly shaped cellular groups in connective tissue which was unaltered except for a slight lymphocytic infiltration. In some places the cells were elongated and gave the appearance of spindle cell sarcoma but there were no embryonic blood vessels present. In other places the cells were prismatic in form and were arranged in regular series, thereby giving the appearance of a basal cell epithelioma. There was no evidence of embryonic canaliculi and there did not appear to be any transition between the cylindric cells of the normal epithelium and the neoplastic cells. This growth was believed to be a case of epithelioma arising from the basal cells of the epididymis. The patient was well one year after the operation.

CASE 20. Hinman and Gibson (16). In a man, 78 years of age, a nodular mass appeared in the left side of the scrotum, 11 months before admission. This was accompanied by a slight drawing sensation. Examination showed the epididymis to be nodular and of a hard rubbery consistence. The skin was adherent. No inguinal glands could be palpated. Operation revealed the tumor to be primary in the body of the epididymis. It was adherent to the skin, the median septum, and the base of the left corpus cavernosum. Epididymectomy was performed.

Microscopically the tumor was composed of fibrous tissue in which were imbedded numerous acini lined by epithelial cells. The basement membrane was lacking in some places. The consensus of opinion was that this growth was an adenocarcinoma of low-grade malignancy. The patient was well 8 months following operation.

CASE 21. Scholl and Verbrugge report the case of a 22 year old man who, 14 months previously, had received a severe kick in the right testicular region. Three months later the testicle became painful and for 6 months before admission steadily increased in size until it reached twice the normal size. During this time he lost 12 kilograms in weight. Examination showed a hard, nodular epididymis associated with hydrocele. At operation, the testicle, epididymis, vas deferens, and their coverings were removed. Three months later he returned with a mass of 2 centimeters in diameter at the lower angle of the incision. This was removed and X-ray treatment was given. Four months later he returned and at this time showed signs of pulmonary involvement.

Microscopically, the epididymis showed a fibrous tissue framework containing numerous spaces filled with atypical epithelial cells arranged in an adenocarcinomatous manner. The testicle was not involved. The vas deferens was involved in certain areas.

The origin of malignant neoplasms of the testicle and epididymis has been a subject for great controversy. One of the outstanding contributions to this subject was made by Chevassu who pointed out the resemblance of the large clear

neoplasm cells to spermatocytes. Chevassu expressed the belief that these cells were derived from the epithelial cells of the seminal tubules. He gave to these neoplasms the name "seminome." Many other investigators, notably Tanner, Nicholson, Debernardi, and Southam and Linell, have referred to these neoplasms as seminomata or spermatocytomata.

The microscopic studies made in the case which forms the subject of this communication reveal the same type of neoplasm as that which commonly arises in the testicle and to which the names seminoma or spermatocytoma have been applied. The fact that this neoplasm had its origin in the epididymis without evidence of any neoplasm in the adjacent testicle would seem to argue against the possibility that such neoplasms have their origin from the germinal epithelium.

Most pathologists are in agreement with Ewing, who states that all of the common neoplasms of the testis are of teratomatous nature, in which one type of tissue usually predominates, to the exclusion of the other teratomatous tissue elements. In many of the neoplasms which have originated in the testicle or epididymis a multiplicity of tissue elements derived from the three germ layers, such as cartilage and bone, skin and accessory skin structures, smooth muscle tissue, fat tissue, brain tissue, placental tissue, remnants of the alimentary or respiratory tract, thyroid tissue, indicate indisputably the teratomatous origin of such neoplasms. Hinman, Gibson, and Kutzmann (15) have found various types of tissue associated with areas of so called spermatocytoma tissue; these authors conclude that "the term 'seminoma' or 'spermatocytoma' must, therefore, be regarded as a misnomer, and the contention of Chevassu is disproved in favor of Ewing's theory." It seems probable that the great majority of cases of primary malignant neoplasm of the testicle and epididymis which have been designated as sarcomata are in fact embryonal carcinomata. The large, spheroidal, spindle-form cells which constitute the essential element of these neoplasms bear a close morphological resemblance to sarcoma cells. True sarcoma of the testicle or epididymis is probably of rare occurrence; Dew's studies lead him to believe that only about 2 per cent of such neoplasms should be regarded as sarcomatous.

The embryonal carcinoma of the testis or epididymis is a rapidly growing neoplasm. In most instances it tends to reach a large size within a short time. Extensive necrosis of the neoplasm cells with hæmorrhage, ulceration, and suppuration is not uncommon. In most instances metastasis occurs relatively early. The most extensive early metastasis occurs along the spermatic lymphatics to the lumbar retroperitoneal lymph nodes. Ultimately, the entire chain of retroperitoneal lymph nodes shows extensive metastasis. In some cases metastasis may involve the tracheomediastinal and cervical lymph nodes. Discontinuous venous metastasis is frequent with the establishment of metastatic tumors in distant viscera.

The embryonal carcinoma of the testis or epididymis is one of the most malignant of all neoplasms. The prognosis is particularly unfavorable in young individuals.

TREATMENT

In view of the fact that metastasis occurs relatively early in these cases, the removal of the testicle, epididymis, and spermatic cord structures is usually of no avail. Hinman (13) has proposed a more radical operation in which, in addition to these procedures, the retroperitoneal and lumbar lymph nodes and lymph channels are dissected away. In the report of the first 46 cases treated in this manner, the operative mortality was 11 per cent. In a later report, Himan (14) states that he has obtained cures in 30 per cent of 79 cases in which the radical operation has been carried out. Cairns (5) reported 74 cases from the London Hospital; 55 of these patients were subjected to simple orchidectomy, while 19 had the radical operation. There was no operative mortality. Thirty-three per cent of the patients on whom orchidectomy was done were said to have recovered, while 31.2 per cent of the patients who had the radical operation were said to have recovered.

The majority of investigators incline to the belief that orchidectomy followed by radium or roentgen therapy offers the greatest hope. The embryonal carcinoma appears to be unusually radiosensitive. Higgins and others have recommended primary treatment with X-ray or radium, to be followed by orchidectomy, which, in turn, is to be followed by a prolonged course of X-ray or radium treatment.

SUMMARY AND CONCLUSIONS

1. The clinical and pathological findings in a case of primary malignant teratoma (embryonal carcinoma) of the epididymis are presented.

2. This neoplasm corresponded structurally to the most common form of malignant neoplasm originating in the testicle. The origin of this neoplasm in the epididymis renders invalid the theory that such neoplasms have their origin in the spermatoblasts of the germinal epithelium.

3. The evidence appears to be conclusive that these neoplasms have their origin in pre-existing teratomata, in which one of the tissue elements undergoes malignant transformation.

REFERENCES

1. BARRINGER, B. S. Report of case of teratoma of epididymis. Internat. J. Surg., 1920, xxxiii, 116.
2. BAZY, P. Sarcome à petites cellulos du corps d'Highmore et de l'épididyme gauche. Bull. et mém. Soc. de chir. de Par., 1892, xviii, 488.
3. Idem. Discussion. Bull et mém. Soc. de chir. de Par., 1893, xix, 481.
4. BLAND-SUTTON, J. An improved method of removing the testicle and spermatic cord for malignant disease. Lancet, 1909, ii, 1406.
5. CAIRNS, H. W. B. Neoplasms of testicle. Lancet, 1926, i, 845–850.
6. CHEVASSU, MAURICE. Tumeurs du testicule. Thèse de doct., Paris, 1906.
7. COLBY, F. Columnar carcinoma of the epididymis. Brit. M. J., 1907, i, 199.
8. DEBERNARDI, LORENZO. Beitraege zur Kenntnis der malignen Hodengeschwuelste. Beitr. z. path. Anat. u. z. allg. Path., 1907, xl, 534–600.
9. DEW, HAROLD. Sarcomatous tumors of the testicle. Surg., Gynec. & Obst., 1928, xlvi, 447–458.
10. EDWARDS, F. S. Cases of small round-celled sarcoma of testicle and spermatic cord. Tr. Path. Soc. Lond., 1887, xxxviii, 221.
11. EWING, JAMES. Neoplastic Diseases. 3d ed. Philadelphia and London: W. B. Saunders Company, 1928.
12. GRASMAN, M. Zur Kenntnis der auf traumatischer Grundlage entstrandenen Hodensarkome. Muenchen, 1900.
13. HINMAN, FRANK. The operative treatment of tumors of the testicle; with the report of thirty cases treated by orchidectomy. J. Am. M. Ass., 1914, lxiii, 2009–2015.
14. HINMAN, FRANK, GIBSON, THOMAS E., and KUTZMANN, ADOLPH A. The radical operation for teratoma testis. Surg., Gynec. & Obst., 1923, xxxvii, 429–451.
15. Idem. Malignant tumors of the testicle. Ann. Surg., 1925, lxxxii, 552–575.
16. HINMAN, F., and GIBSON, T. E. Tumors of the epididymis, spermatic cord and testicular tunica. A review of the literature and report of three new cases. Arch. Surg., 1924, viii, 100.
17. HIGGINS, C. C. Malignant tumors of testicle. Ann. Surg., 1928, lxxxvii, 263–291.
18. KELLER, O. Les tumeurs malignes du testicle. Arch. de mal. d. reins., 1929, iii, 579.
19. KOCHER, T., and LANGHANS. Die Krankheiten der maennlichen Geschlechtsorgane. Deutsche Chirurgie. 1887, l, b, 508, 526.
20. KOLSTER, R. Sarcoma der Epididymis mit Metastasen im Mediastinum. Arch. f. path. Anat., 1899, clv, 388.
21. LA POINTE, A., and CAIN, A. Epitheliome de l'epididyme. Bull. et mém. Soc. de chir. de Par., 1923, xlix, 391.
22. LARSON, L. W. Embryonal carcinoma of the testicle. J. Lab. & Clin. Med., 1930, xv, 332.
23. LENTE, F. D., and JACOBUS, A. M. Cystic chondrosarcoma of the epididymis. Tr. New York Path. Soc., 1881–1882, iv, 119.
24. MIYATA, T. Zur Kenntnis der Hodengeschwuelste und die Bedeutung des Traumas fuer ihre Entstehung. Arch. f. klin. Chir., 1918, ci, 426.
25. NICHOLSON, G. W. New growths of the testicle. Guy's Hosp. Rep., 1907, lxi, 249–321.
26. ROWLANDS, R. P., and NICHOLSON, G. W. A case of primary squamous-celled epithelioma of the epididymis. Lancet, 1909, i, 304.
27. RUSSELL, W. B., and WOOD, F. L. Sarcoma of the epididymis; removal. Brit. M. J., 1899, ii, 1193.
28. RYDYGIER, L. Ein Fall von primaerem Melanosarkom des Nebenhodens. Arch. f. klin. Chir., 1891, xlii, 769.
29. SAKAGUCHI, Y. Ein Fall von Primaerem Karzinom des Nobenhodens. Frankfurt. Ztschr. f. Path., 1914, xv, 62.
30. SCHOLL, A. J., and VERBRUGGE, J. Adeno-carcinome primitif de l'epididyme (avec relation d'un cas personel). J. d'urol., 1929, xxvii, 24.
31. SOUTHAM, A. H., and LINELL, E. A. The pathology of neoplasms of the testis. Brit. J. Surg., 1923, xi, 223–233.
32. SPANDRI, P. Chondro-sarcoma dell' epididymo. Riv. veneta di sc. med., 1904, xli, 167.
33. TANNER, CHESTER O. Tumors of the testicle; with analysis of one hundred original cases. Surg., Gynec. & Obst., 1922, xxxv, 565–572.
34. WROBEL, A. Beitraege zur Kenntnis der malignen Hodengeschwuelste. Breslau, 1902.

EDITORIALS

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CARL LANGENBUCH AND THE FIRST CHOLECYSTECTOMY

THE fiftieth anniversary of the first cholecystectomy will be celebrated on July 15, 1932. Carl Langenbuch performed the first operation in 1882, and his name has been permanently engraved thereby in medical history.

The events leading to the first cholecystectomy arose in the preliminary work of Teckof who first removed the gall bladder of a dog in 1667. Ettmueller repeated Teckof's work in 1670, and Herlin one hundred years later confirmed Teckof's observations by the removal of the gall bladder in cats. Joenisius had removed stones from a biliary fistula in 1676, and Vogel and Bloch in 1774 sectioned a biliary sinus to remove some calculi. Recamier in 1826 introduced a trocar into the gall bladder for drainage purposes, and in 1849 he repeated this operation successfully. In 1858 Santopadre performed the first cholelithotripsy.

Jean Louis Petit in 1743 performed the first cholecystostomy through adhesions which he had artificially created, and in 1867 Bobbs performed the first cholecystotomy. Bobbs' operation was accidental, inasmuch as the correct diagnosis was not made before operation, yet his operative procedure was a new achievement which successfully relieved the patient. Sims in 1878 published a report of the first intra-abdominal cholecystostomy which he performed, and thereafter numerous authors reported variations of cholecystotomy and cholecystostomy until the time of Carl Langenbuch's memorable surgical achievement of cholecystectomy in 1882.

Langenbuch reasoned that as some humans had been born without a gall bladder, and as the elephant and horse do not normally possess this organ, the removal of the gall bladder in man should not be injurious. Therefore as there was no physiological contra-indication to the operation, he developed an operative method by studies upon six cadavers. Langenbuch finally evolved a technique and recommended exploration of the abdominal cavity through a T-incision, the horizontal bar being a transverse incision through the upper part of the right half of the abdomen while the longitudinal incision followed the outer border of the right rectus muscle. Each incision varied from 10 to 15 centimeters in length. The colon and the intestines were pushed downward by means of a large, flat sponge. The right lobe of the liver was raised through the abdominal wound until it protruded. The under surface of the liver was then secured between the fingers of the left hand and the gall bladder was identified with the right. The gall bladder was then freed from the liver by blunt, finger dissection and silk ligatures were applied around the lower end of the gall bladder somewhat above the cystic duct. This

was accomplished after exposure of the neck of the gall bladder by knife and scissor dissection of the peritoneal coat. The section was then made between ligatures. Langenbuch stated that if the gall bladder was full it could be emptied by aspiration to prevent possible rupture or injury to the sac during cholecystectomy. The abdominal wall was then closed, layer by layer.

On July 15, 1882, Langenbuch performed the first operation upon man. The patient was a 43 year old male upon whom extreme precautions were taken to assure asepsis. The operation was carried out as described and the patient got along very well. Two days after the operation he began to take liquid diet and twelve days after the operation he left his bed to be dismissed from the hospital about six weeks later. One of the most interesting observations in relation to his first cholecystectomy was his statement that he removed, rather than drained the gall bladder, not only because it contained stones but because it was the type of gall bladder in which stones would re-form.

The performance of the first cholecystectomy leads one to inquire into the life of the great man who first evolved this operation. Carl Langenbuch was born on April 20, 1846, at Kiel. He studied at Kiel and Berlin and graduated from the latter city in 1869. Immediately thereafter he went to the Franco-German war for a short period and came home as assistant to Schuler von Willms in Bechanien under whom his surgical training was developed. When only twenty-seven years of age he was made surgical assistant at the Lazarus-Krankenhaus in Berlin where he remained until his death, and in which place he laid the foundations of his versatile and varied career. It is no wonder that he loved this hospital in which he practiced his art, for it was here that he developed his reputation which brought credit not only to himself but also to his hospital. Indeed it is largely through him that the Lazarus-Krankenhaus became the greatest in Berlin. Langenbuch's vision was extensive and his work produced a widespread influence upon the surgical world. At the age of forty-five he published a "Clinical Treatise on Surgery of the Liver and Gall Bladder" which became the handbook and standard work in this subject.

Early in 1880 he began to section peripheral nerves and even trunks in the spinal cord for tabes, and he performed a considerable amount of experimental work in relation to this disease. He resected a large part of the liver for carcinoma (the piece weighing 400 grams), and he performed a laryngotomy in 1880. In 1886 he went to the Russo-Turkish war against Bulgaria where he became an ardent military surgeon and where he developed the specialty of veterinary surgery. He published works on the stretching of nerves, on diseases of the spinal cord, the treatment of gall stones, the treatment of severe hæmorrhage by the application of zinc chloride, and numerous works upon military and veterinary surgery. He was without fear as a surgeon, and he had an unusual grasp of the symptoms necessitating operative interference.

He possessed a gentle and timid nature but had a quiet jocularity that endeared him to everyone. He cultivated an interest in politics and had a natural curiosity for things of a social character. He was extremely patriotic and had musical inclinations which balanced and protected him from the one-sidedness of medicine. He lived happily and, fortunately, long enough to enjoy the admiration of his colleagues for the excellent and unusual work that he had done. In like manner he lives in the memory of the present day, probably glorified more now than before, and rightfully so, for time has proved the merit of his work. The

multiplicity of operations performed upon the gall bladder about Langenbuch's time are receding in popularity, but Langenbuch's operation of cholecystectomy remains steadfast, if not indeed the established and preferred operation.

Langenbuch's life and his greatest achievement, i.e., his cholecystectomy, furnish us an excellent example of the progress that personal character and painstaking experimental work produce in the development of new methods in surgery. STANLEY H. MENTZER

MEMOIRS

WILLIAM WILLIAMS KEEN

JANUARY 19, 1837—JUNE 7, 1932

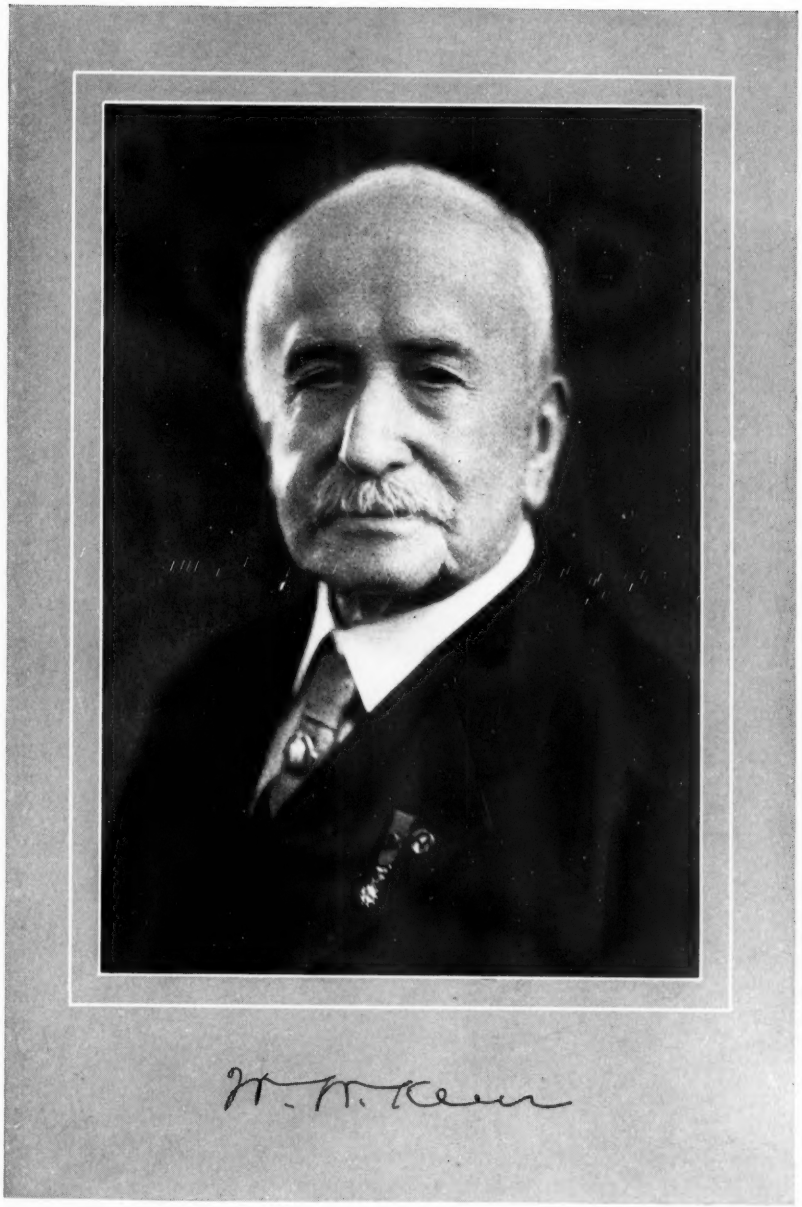
> "*I believe in God and in Evolution.* To all sincere seekers after truth: who revere the Bible as the word of God; who revere nature as the work of God; and who believe that rightly interpreted they must surely agree. . . . To develop great men . . . and then by death to quench them in utter oblivion would be unworthy of Omnipotence. To my mind, it is simply an impossible conclusion. Man's soul *must* be immortal." W. W. Keen.

THE death of this eminent surgeon—the lover of his personal God, a patriotic fighter for his beloved country, who wore its uniform in two wars (in the Great War at the age of eighty years)—has brought the whole thinking world to attention in admiration of a fine and useful life, and the profession of medicine mourns with deep sorrow the passing of a beloved comrade. His was a devoted service of seventy years in the practice of the great learned profession—scientific medicine. He was an ardent supporter of every moral, scientific, and progressive advance in civic, state, and national affairs.

The American College of Surgeons and its official journal, SURGERY, GYNECOLOGY AND OBSTETRICS, acknowledge a personal loss. Dr. Keen was the first surgeon of our country to accept and have conferred upon him an Honorary Fellowship in the College. He contributed to many of its scientific meetings, and lent his inspiring presence at numerous of its annual sessions. He was an early subscriber and a frequent contributor to the columns of the Journal. In the Great War—the eldest member of the Medical Reserve Corps—he was a personal friend. By his pen, his personal contacts, his orations, and his friendly advice he was an inspiring aid to those of us who had to do with enrollment for war.

During his span of life—ninety-five years—his was the rare privilege of witnessing and participating in every advance in surgery, and of knowing all of the great men in medicine of his day. He began his medical studies in the Fall of 1860, and graduated in March, 1862. He early "declined to be a champion of the Past" but assumed the rôle of "a Herald of the Dawn." In 1922, in his oration delivered on the occasion of the conferring upon him of the Bigelow Medal, he took as his theme *Sixty Years of Surgery*.[1] He compared the poverty of knowledge

[1] Boston M. & S. J., 1922, clxxxvii, 592–600.



and meagerness of resources in the 60's with the wealth of both in 1922, and said he wished he could "return in 1982 to converse with the Bigelows, the Grosses, the Mayos, the Flexners, and the Lovetts of that wonderful day." The first operation he ever saw was the removal of an upper jaw by Joseph Pancoast, and his first operative case—in the days of the Indian wars—removal of an arrow which had penetrated deeply just below the left eye. He was office student of Jacob DaCosta and John Brinton while he studied at Jefferson Medical College.

Sworn into service as assistant surgeon in Washington, July 4, 1861, he witnessed actual warfare in the Battle of Bull Run. Just after the Civil War he was a pupil in Paris of Pouchet, son of Pasteur's opponent. In 1865 he was a pupil in Virchow's laboratory. On the occasion of Lister's visit to Philadelphia in 1876, Keen became fully converted to Lister's views.

Keen's course of lectures at Jefferson on *Pathological Anatomy* in 1866–1867 was the first ever given in Philadelphia. The first official course in surgical pathology was authorized in 1897. In the 60's assistants in the dissecting room often came directly to the surgical clinics to assist in operations. Pancoast, Gross, and all others "operated in discarded, blood-stained coats, the veterans of a hundred fights." The teaching faculty consisted of seven professors and one demonstrator—anatomy. There were no ward classes. At Jefferson, they had two rooms, with five or six beds each, for the most serious cases.

The first laboratory of research in the United States was established in 1884. As late as the 80's there were in most hospitals no trained nurses. The first clinical thermometer he ever saw was brought to him from London in 1876 by Weir Mitchell. Of the blood, knowledge was most primitive. The electrocardiograph was not even a dream; no radium and no X-rays; no knowledge of test meals. Until the 80's or 90's, smallpox was the only enemy combated by vaccination. There were no serums, and no knowledge of how to prevent tetanus, diphtheria, malaria, yellow fever, and other diseases. The real cause of tuberculosis was not known until 1882. Protective measures for the well were not even thought of; there was no knowledge of bacteria and bacteriology. Vaccination, anæsthesia, and antisepsis (including bacteriology), Keen rated as "the three greatest blessings in the realm of medicine conferred on man since the Christian era began," and Lister's genius in applying Pasteur's discoveries to surgery "wrought the greatest revolution surgery has ever witnessed."

Nothing was known of endocrine glands and their important functions, nor of hormones and their mechanism. There was no Schick test, Noguchi test, Pirquet test, Wassermann reaction, etc. Nothing was known of the spread of diseases by the fly, the flea, the mosquito, the louse, the rat, and the cattle tick. So-called sanitation was ineffective, because bacteria were unknown.

In the operative surgery of Keen's surgical youth he listed amputations, ligation of arteries, occasional excision of joints, removal of external tumors,

ovariotomy, cutting for stone in the bladder. Gall stones were first removed from the gall bladder by Bobbs, of Indianapolis, in 1867. Goiter operations were infrequent. Ophthalmology and the other specialties were just becoming visible. Surgery of the head, the chest, and the abdomen was rare. The cause of appendicitis was not known until 1886. There was occasional plastic surgery. In 1895 diphtheria antitoxin was discovered. Operations for quiescent hernia were rare.

Instruments were not disinfected; there were no artery forceps. Absorbable catgut ligatures were intoduced by Lister in 1869. There were no modern retractors, and hypodermic syringes and the aspirator were not in general use until toward the end of the Civil War. Gauze "sponges" came into general use in the late 70's or early 80's, prior to which only marine sponges were used, both in clean and in suppurating cases. In dislocations of the hip, and sometimes of the shoulder, the "barbarous block and pulley" were used. Fractures of the base of the skull were almost uniformly fatal. "Mastoid disease" was unknown by Gross and Erichsen, in 1859. Cerebral localization was foreshadowed by Hughlings Jackson in 1867. Localization and subsequent removal of a tumor of the spinal cord were first described by Gowers' and Horsley in 1888. Chevalier Jackson was not born till 1865. "In the chest, the heart lies in a straight line only one inch from the surface, yet, as Frederic Lee has strikingly said, it took surgery, with laggard step, twenty-four centuries to travel that one inch." "Imagine, if you can," said Keen, "the forlorn condition of the doctor sixty years ago—without everything except his eyes, his ears, and his fingers; then you can appreciate the triumphal march of medicine during a single lifetime."

Dr. J. Chalmers DaCosta, Keen's successor as professor of surgery in Jefferson in 1907, said of him: "Dr. Keen was always calmer, quieter, kinder, pleasanter, the worse the surgical situation was, and I never saw it get the best of him."

Dr. Keen was a great teacher. He once said: "I always feel at the Jefferson Hospital as if I were on the run with a pack of lively dogs at my heels. Students are the best whip and spur I know." He was a great man, a great American, a great surgeon, and the beloved dean of our medical profession. He knew the joy of living. The "wondrous love of God for Man and the final lofty destiny of the Human Race" was to him "the most impressive, the most inspiring thought of all the ages." In speaking to a group of graduates, he said: "If in your own life you realize the characteristics of the ideal physician . . . if you attain to old age, when the hairs whiten and the crow's feet begin to show, when your natural forces are abated, you will then not be alone in the world, but will have honor, love, obedience, troops of friends, and one Friend above all others, the Great Physician." We know this was and is his reward. The world is a better place for his having been here. His monument is built in the hearts of his thousands of friends, and his memory will live on through the ages. FRANKLIN H. MARTIN.

William Williams Keen was born in Philadelphia, January 19, 1837, the son of William W. and Susan (Budd) Keen. In 1867, he married Emma Corinna Borden, of Fall River, Massachusetts, who died in 1886. His children, all of whom survive him, are Corinne (Mrs. Walter J. Freeman), Florence, Dora (Mrs. George W. Handy), and Margaret (Mrs. Howard Butcher, Jr.).

Degrees received include A.M., Brown University, 1859; M.D., Jefferson Medical College, Philadelphia, 1862; Sc.D., 1912; LL.D., from Brown in 1891, Northwestern and Toronto in 1903, Edinburgh in 1905, Yale in 1906, St. Andrews in 1911, and Pennsylvania in 1919; Ph.D. from the University of Upsala in 1907; Sc.D. from Harvard in 1920; Doctor, *honoris causa*, University of Paris, 1923.

After study in Europe during 1864–1866, he established himself in practice at Philadelphia. During 1866–1875 he conducted the Philadelphia School of Anatomy; lecturer in pathological anatomy at Jefferson Medical College, 1866–1875; professor of artistic anatomy, Pennsylvania Academy of Fine Arts, 1876–1889; professor of surgery, Woman's Medical College, 1884–1889; professor of surgery, Jefferson Medical College, 1889–1907, and professor emeritus from 1907.

Assistant surgeon U. S. Army in 1861, and acting assistant surgeon 1862–1864. He volunteered for the Spanish-American War, but owing to its short duration, his services were not required; 1st Lt., M. R. C., U. S. A., 1909; major, 1917–18. Member of the National Research Council 1917–18.

Charter trustee, Crozer Theological Seminary, from 1867; trustee and fellow, Brown University, from 1873; president, American Surgical Association, 1899, American Medical Association, 1900, College of Physicians, Philadelphia, 1900–1901, International Congress of Surgery, Paris, 1920 (the first American to hold the office), Congress of American Physicians and Surgeons, 1903, American Philosophical Society, 1907–1917; honorary fellow, Royal College of Surgeons of England, Edinburgh, Ireland, Italian Surgical Society, American College of Surgeons; associate fellow, American Academy of Arts and Sciences; honorary fellow, Boston Surgical Society (awarded Bigelow gold medal); awarded Colver-Rosenberger medal of honor, Brown University; gold medal by Pennsylvania Society of New York. Officer, Order of the Crown of Belgium, 1920; officer, Légion d'Honneur, France, 1923; member, Founders and Patriots of America, Loyal Legion, Medical Veterans of the World War, Sigma Xi.

Author of *Reflex Paralysis, and Gunshot Wounds and Other Injuries of Nerves* (both with Weir Mitchell and Morehouse), 1864; Keen's *Clinical Charts*, 1870; *History of the Philadelphia School of Anatomy*, 1874; *Early History of Practical Anatomy*, 1870; *History of the First Baptist Church of Philadelphia*, 1898; *Surgical Complications and Sequels of Typhoid Fever*, 1898; Addresses and Other Papers, 1905; *Animal Experimentation and Medical Progress*, 1914; *The Early Years of Brown University, 1764–1770*, 1914; *Ether Day Address*, 1916; *Treatment of War Wounds*, 1917; *Surgical Operations on President Cleveland*, 1917; Colver Lectures at Brown University on "Medical Research and Human Welfare," 1917; Selected Papers and Addresses, 1922. Editor: Heath's *Practical Anatomy*, 1870; *Diagrams of the Nerves of the Human Body*, by W. H. Flower, 1872; American Health Primers, 1879–1880; Holden's *Medical and Surgical Landmarks*, 1881; Gray's *Anatomy*, 1887; American *Text-Book of Surgery*, 1892, 1903; *I Believe in God and in Evolution*, 1922; *Everlasting Life*, 1924; Keen's *System of Surgery*, 1906–21.

For much of the material contained in the above sketch, I am indebted to Dr. Keen's writings, to *William Williams Keen* by Wilfred Pickles, M.D., of Providence, Rhode Island (Rhode Island M. J., 1927, x, pages 1–10), and to *Who's Who in America*.

EARLY AMERICAN HOSPITALS

THE PENNSYLVANIA HOSPITAL OF PHILADELPHIA

FRANCIS R. PACKARD, M.D., PHILADELPHIA, PENNSYLVANIA

THE Pennsylvania Hospital was chartered by the Provincial Assembly of Pennsylvania in 1751, and claims to be the oldest hospital established as such in the British Colonies in North America. There are several institutions which are now great hospitals, notably the Philadelphia General Hospital (1731) and Bellevue Hospital in New York (1735), which date their founding prior to that of the Pennsylvania, but they were established as poorhouses or almshouses and shelters for the aged and dependent, and only became hospitals in the modern sense of the term many years later.

The story of the founding of the Pennsylvania Hospital is concisely related by Benjamin Franklin in his *Autobiography*. He ascribes the credit of originating the idea to Dr. Thomas Bond, a distinguished physician of Philadelphia. Bond had endeavored to raise funds by private subscription for the purpose. He had not approached Franklin because he thought it out of his line. However, as all those to whom he spoke asked him what Franklin thought about it, he finally determined to consult him. Franklin at once gave him his hearty co-operation, and his political and personal influence to get a charter and raise money, and Bond's project was soon realized. The administration was placed in the hands of a Board of Managers, twelve in number, elected from among the contributors. Joshua Crosby, a wealthy merchant, was elected the first president and Benjamin Franklin, clerk of the Board. When Crosby died in 1755 Franklin succeeded to his office.

The hospital was opened for patients in February, 1752, in a house rented from the estate of Judge Kinsey, on the south side of High (now Market) Street below Seventh. It is curious to find the Managers adopting measures to provide occupation for such patients as could be employed, the modern "occupational therapy," at an early date, providing large and small spinning wheels, two pairs of cards, and wool and flax "to employ such patients as may be capable of using the same." The first medical staff was composed of Drs. Thomas and Phineas Bond, and Lloyd Zachary, with "Drs. Graeme, Cadwalader, Moore, and Redman to assist in consultation on extraordinary cases." Benjamin Franklin and Thomas Bond devised a seal for the hospital. It bore a device of the Good Samaritan relieving a sick man, with the inscription "Take care of him, and I will repay thee." The seal was made by a silversmith in Boston and remained in use until 1833, when, being worn out, it was broken and a new one bearing the same design and inscription substituted for it.

The hospital soon outgrew its temporary quarters and the Managers purchased a permanent site on which to build on Pine Street between Eighth and Ninth streets. Some years later (1767) the Penn family donated to them a strip of land along Spruce Street, which thus provided the hospital with the entire block, which it occupies to the present day. The cornerstone of the buildings for the hospital was laid on May 28, 1755, with Masonic ceremonies. It is exposed in the wall and bears the following inscription, composed by Benjamin Franklin:

IN THE YEAR OF CHRIST

MDCCLV

GEORGE THE SECOND HAPPILY REIGNING

(FOR HE SOUGHT THE HAPPINESS OF HIS PEOPLE)

PHILADELPHIA FLOURISHING

(FOR ITS INHABITANTS WERE PUBLICK SPIRITED)

THIS BUILDING

BY THE BOUNTY OF THE GOVERNMENT

AND OF MANY PRIVATE PERSONS

WAS PIOUSLY FOUNDED

FOR THE RELIEF OF THE SICK AND MISERABLE

MAY THE GOD OF MERCIES

BLESS THE UNDERTAKING.

By December 17, 1756, all the patients had been removed from the old quarters into the new building, the wards of which have been occupied continuously ever since.

The records of the patients admitted to the hospital have been carefully preserved and some of the earlier ones are most interesting. Among them we find patients admitted who had been injured by hostile Indians. Thus "March 21, 1756, admitted David Howell, a poor patient from Berks County, having a Gunshot wound and fractured Bone in one Arm done the 6th inst. by the Enemy Indians"; and "October 3, Margaret Sinclair, a poor patient, with Disiness in the Head having been much abused by the Indians." On October 13, 1755, "Michael Higgins, a Soldier, was admitted, having his underjaw shot off in the late Engagement under General Braddock," and there are entries of many other admissions of soldiers injured during the continuance of the war with the French and Indians.

During the Revolution the hospital underwent some serious vicissitudes. At the outset it was utilized by the Americans but during the British occupation of Philadelphia from September, 1777, to May, 1778, it was taken over by their medical department. When the Americans regained the city the medical department of the Continental Army rented the "Elaboratory" of the hospital for the purpose of preparing medical supplies, and made arrangements for the admission of a number of soldiers on a paying basis to its wards.

On December 31, 1790, Mrs. Stephen Girard, the wife of the rich banker and philanthropist, was admitted as a lunatic pay patient. On March 3, 1791, she gave birth to a daughter, who was put out to nurse by the Hospital Managers, with one John Hatcher's wife. The child died on August 26, 1791, and the funeral expenses were paid by the steward of the hospital. Mrs. Girard died on September 13, 1815. She was buried on the hospital grounds but the exact location of her grave has never been found. Although there are several other entries in the Minutes showing that occasional accouchements occurred in the wards of the hospital, a lying-in department was not opened for many years. In 1793 a legislative act was passed authorizing the hospital to establish such a department, but no further action was taken until 1803, when the Managers formally announced the opening of a lying-in department in the hospital. In 1807 the First Troop of Philadelphia City Cavalry gave the hospital the pay which it had just received from the United States Government for its services during the Revolution, the money to be applied

Inscription on cornerstone of buildings for hospital, laid May 28, 1755.

to "the purpose of a Lying-In and Foundling Hospital." No special medical officer was assigned to the department until 1810, when Dr. Thomas Chalkley James was appointed physician to the lying-in department. Drs. Hugh L. Hodge and Charles D. Meigs were both physicians to this department in the forties and fifties during the height of their controversy with Oliver Wendell Holmes on the subject of puerperal fever. The record of the various changes in the location of the lying-in ward is a sufficient index of the contagiousness of puerperal fever. It was opened on the second floor of the East Wing in 1803. In 1817 it was moved to the apartment known as the Contributors' Room, from which it was changed to the second story of the Centre Building in 1824. In 1830 the physicians directed attention to a renewed prevalence of puerperal fever and the lying-in department was ordered closed. Some months later after thorough cleansing and disinfection it was re-opened, but in 1839 it was necessary to move it once more, this time to the Picture House, a small isolated building on the hospital grounds. Here it remained until 1851 when the staff decided that puerperal fever had become endemic, and the ward should be closed. The department was finally abandoned altogether in 1854. A few years ago the Philadelphia Lying-In Hospital was merged in the Pennsylvania Hospital, so that the institution has now a splendidly equipped modern obstetric hospital.

It is noteworthy that the three members of the first medical staff of the Pennsylvania Hospital, the two Drs. Bond and Lloyd Zachary had all finished off their medical education by study abroad. All of them were men of the highest professional standing and their successors maintained the reputation of the staff and kept the work of the hospital on the highest plane. A brief enumeration of some of those elected to the staff will suffice to show the truth of this assertion. To John Morgan and William Shippen, Jr.,

House of Employment, Alms House, and Pennsylvania Hospital. (From engraving by Hulett.)

belong the honor of holding the first two chairs in the first medical school founded in the British Colonies, that of the University of Pennsylvania, founded in 1765. Adam Kuhn, the third professor to occupy a chair in the medical school was also physician to the hospital for many years. Benjamin Rush, a signer of the Declaration of Independence, a pioneer in the proper treatment of mental diseases, and the best known medical teacher of his day, was constant in his attention to his duties at the hospital from his election to the staff in 1783 until his death in 1813. Caspar Wistar, the author of the first American anatomical textbook, and in whose memory the famous Wistar Parties are yet given by members of the American Philosophical Society, was a member of the staff for seventeen years. Philip Syng Physick, the most famous surgeon of his day in America, served on the staff from 1794 until 1816. All of these men had received the degree of M.D. from the University of Edinburgh and they all exerted a powerful influence on medical teaching and practice in their day. Of their successors I might recall the names of John C. Otto, who wrote the first report of the occurrence of the hæmophilic diathesis in a family; John Rhea Barton, the inventor of the Barton bandage and of the "bran dressing" for fractures; Hugh L. Hodge and Charles D. Meigs, the two eminent obstetricians whose memory is unfortunately forever linked with their erroneous views on puerperal fever; George B. Wood, the first editor in collaboration with Franklin Bache, of the *United States Dispensatory* and William Wood Gerhard, who established the essential difference between typhus and typhoid fevers.

In 1766, the year after the establishment of the medical school, Thomas Bond began giving courses of clinical lectures in the hospital, the first given in this country.

In 1773 the hospital began taking "apprentices." They served 5 years and at the end of that time, if their services had been satisfactory they were given a certificate and a suit of "cloathes." These young men lived in the hospital and their duties corresponded closely with those of the present day internes, although they were not graduates in medicine. In 1824 the Managers began the practice of taking young medical graduates as resident physicians. The first two, appointed in that year, were Caspar Wistar and Caspar Morris.

It is impossible to find out just where operations were performed in the early years of the hospital as there is no mention of any special operating room in the records until 1804, when a clinical amphitheatre was constructed on the third floor of the Centre Building. This room, though the lower part is now used for other purposes, still contains the upper tiers of benches from which students must have witnessed operations by Physick, and heard the lectures of Benjamin Rush, and the other great men of the past. In 1869 a new amphitheatre was constructed and the old one abandoned. The second amphitheatre in turn was replaced by a handsome modern operating theatre in 1896.

From its foundation to the present day the Pennsylvania Hospital has extended the use of its wards for teaching purposes. The staff was authorized by the Managers to bring their apprentices or students into the wards, and other students could obtain admission to the operations and clinics at the hospital by the payment of certain fees. In 1762 Dr. John Fothergill, the famous Quaker physician of London, presented

Pine Street front of the hospital engraved by Tucker, 1820.

the hospital with a set of anatomical and obstetrical casts and pictures. The latter had been painted by Van Rymsdyk, the celebrated Dutch anatomical artist, living in London, who had made most of the illustrations for William Hunter's great book on *The Gravid Uterus*. They cost Dr. Fothergill 200 guineas. He sent them over to the hospital in the care of Dr. William Shippen, Jr., who was returning to America after the completion of his medical studies abroad, and had discussed with Dr. Fothergill during his sojourn in London his plans for giving courses in anatomy and midwifery in Philadelphia, and Fothergill wrote the Managers that he hoped his gift would be of use to Shippen or other teachers as he realized that there would be difficulty in procuring bodies for dissection. Shippen had been a pupil of William Hunter in London—the first teacher of anatomy in London to adopt what was known as the "French method" of teaching anatomy, namely providing human corpses for his students actually to dissect, instead of relying on the use of models, casts, and pictures. Although Shippen certainly used the Fothergill casts and pictures we know that he managed to procure bodies for his students to dissect, as he wrote in a published statement that he had received from the judges the bodies of executed criminals, and had also procured some from the Potter's Field.

In 1762, Dr. John Fothergill again showed his interest in the hospital by presenting it with a book entitled *An Experimental History of the Materia Medica*, by William Lewis, F.R.S., "for the Benefit of the Young Students in Physic who may attend under the direction of the Physicians." In 1763 the physicians to the Hospital furthered this idea by presenting the following resolution to the Managers:

"As the Custom of most of the Hospitals in Great Britain has given such gratuities from those students who attend the Wards of the Hospital to the Physicians and Surgeons attending them, we think it properly belongs to us to appropriate the Money arising from thence. And we propose to apply it to the founding of a Medical Library in the Hospital which we judge will tend greatly to the Advantage of the Pupils and the honor of the Institution." This proposal was accepted by the Managers who agreed to provide suitable accommodations for the books, and thus began the first public medical library in this country. Shortly after the library received a number of valuable books from the estates of Dr. Benjamin Morris and Dr. Lloyd Zachary. William Strahan, the London publisher, in 1774, made a donation of books to the value of one hundred pounds. In 1790 the Managers requested Dr. John Coakley Lettsom, of London, to

select and purchase medical books for the library. Dr. Lettsom not only expended most judiciously the money sent him for this purpose, but also donated many books to the library. For many years the library continued to grow and was much used but in the later years of the Nineteenth Century the rapid growth of the Library of the College of Physicians soon surpassed it. In 1893 it contained 14,812 volumes, including a number of medical incunabula, many valuable herbals, and classic medical works, and complete sets of most of the older medical journals, such as the *Lancet* and the *American Journal of the Medical Sciences*.

From its foundation provision was made in the hospital for the care of insane patients. In 1841, a separate department was created for this branch of its work, located on a large tract of land purchased by the Managers for this purpose, in West Philadelphia. From the opening of this department until his death in 1883, Dr. Thomas S. Kirkbride was its physician in chief and superintendent. In the minds of the public this long association led to the bestowal of his name as a synonym for that of the hospital and to many persons "Kirkbride's" was more generally known than the Department for the Insane of the Pennsylvania Hospital.